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Pathology

EXPERIMENTAL PATHOLOGY

300. The Nature of Gliomas as Revealed by Animal Experimentation

H. M. ZIMMERMAN. *American Journal of Pathology* [*Amer. J. Path.*] **31**, 1–29, Jan.–Feb., 1955. 23 figs., 9 refs.

A discussion of the different classifications of gliomata is followed by brief case reports exemplifying the problems in diagnosis, especially the difficulty of determining the nature of the whole glioma by examination of a small biopsy specimen. In each case the biopsy material suggested that the growth was a relatively benign astrocytoma or ependymoma, but subsequent post-mortem examination revealed the presence of a malignant glioblastoma. The author considers that very few gliomata consist of one cell type only and that considerable caution is therefore necessary in assessing the relative malignancy of such tumours from portions removed at operation.

In a number of experiments on mice, tumours resembling gliomata were produced by implanting tiny pellets of chemical carcinogens (especially methylcholanthrene) into the brain. Most of these tumours consisted of several cell types; for example, in one animal part of the tumour was composed of spongioblasts and part consisted of an oligodendroglioma. In another experiment extracts of a single primary brain tumour were implanted into two series of animals. In one series an oligodendroglioma developed which was transplanted through 100 animals and remained a "pure" oligodendroglioma throughout. In the other series, from extracts of the same primary tumour, an ependymoma developed which also remained constant through 100 transplants. These experiments suggest, according to the author, that glioma cells are multipotential—that is, they can develop into one or other of several types of tumour according to certain determining factors, the most important of which is the position of the tumour in the brain. In further experiments it was found that when the chemical carcinogen was placed in the ventricular system an ependymoma or an ependymoblastoma developed; when it was placed in the subcortical white matter a glioblastoma resulted; in the occipital lobes an oligodendroglioma was most common; in the corpus callosum a spongioblastoma polare; and in the cerebellum a medulloblastoma. The distribution of these experimentally produced tumours closely resembled that of the various types of glioma found in man. The author therefore concludes that the environment of multipotential glioma cells in the brain is of first importance in determining the type of tumour which develops, but he also considers that external factors—such as irradiation of the tumour—may influence the histological appearances and the rate of growth.

Ruby O. Stern

301. Experimental Studies on the Spread of Cancer in the Lymphatic System. II. Absence of a Lymphatic Supply in Carcinoma

I. ZEIDMAN, B. E. COPELAND, and S. WARREN. *Cancer* [*Cancer* (*N.Y.*)] **8**, 123–127, Jan.–Feb., 1955. 13 figs., 9 refs.

Experiments were designed to determine whether or not carcinoma has a lymphatic supply. The transplantable V2 carcinoma was used in domestic rabbits. A tumour suspension was injected into afferent lymphatics to produce cancer in the corresponding nodes. Later tracer substances, radiogold or Berlin blue, were injected into these afferent lymphatics. The localization of the tracer substances was then determined. It was found that the cancer, growing within and also outside the lymph node, was not significantly penetrated by the tracers.

It is concluded that V2 carcinoma has no demonstrable lymphatic vascular supply. The available evidence strongly suggests that lack of a lymphatic supply may be characteristic of carcinoma.—[Authors' summary.]

302. The Influence of Irradiation of the Brain on the Development of Epitheliomata in Mice. (Влияние облучения головного мозга на возникновение индуцированного кожного рака у мышей)

S. N. ALEKSANDROV. *Бюллетень экспериментальной Биологии и Медицины* [*Byull. eksper. Biol. Med.*] **39**, 52–56, Jan., 1955. 3 figs.

In this study an area of the skin of 150 mice was painted with a 0·1% benzol solution of 9:10-dimethyl-1:2-benzanthracene two or three times a week for 4 months. After the first 2 months two out of three groups of animals (50 mice in each) were subjected to *x*-irradiation at 10-day intervals, each dose consisting of 350 r, the total dose for ten irradiations thus being 3,500 r. Irradiation was limited to the head in the first group and to one hind leg in the second, the third group acting as a control.

All three groups of mice developed papillomata in a similar proportion of cases (nearly 100%). However, the average size of the tumour and the age at which

malignant change took place were different in Group 1 from those in Groups 2 and 3. In Group 1 the size was small, there was a definite period of temporary regression, and malignant change took place later; there was no significant difference between Groups 2 and 3. In further studies irradiation given simultaneously with the application of the carcinogen had no effect on the time of onset of malignant change, while doubling the dose of *x* rays appeared to hasten rather than to retard malignant change (the dose, however, was so toxic that the animals died between 110 and 120 days after the beginning of the experiment).

The author concludes that irradiation of the brain may retard the onset of malignant change in induced tumours. *A. Swan*

303. **Experimental Amoebic Infection of the Liver in Guinea-pigs. I. Infection via the Mesenteric Vein and via the Portal Vein. II. Abscess Formation in Animals with Persistent Intestinal Lesions**

B. G. MAEGRAITH and C. HARINASUTA. *Annals of Tropical Medicine and Parasitology* [*Ann. trop. Med. Parasit.*] 48, 421–433 and 434–441, Dec., 1954. 12 figs., 25 refs.

It has been generally accepted, although never definitely proved, that extra-intestinal amoebiasis must be the result of amoebic metastasis arising from an intestinal lesion. In an attempt to confirm this the authors have carried out experiments at the Liverpool School of Tropical Medicine to determine whether amoebic infection of the liver could be produced by injection of suspensions of *Entamoeba histolytica* into the mesenteric and portal veins of guinea-pigs; a control group of animals received injections of amoeba-free inoculum. Hepatic lesions were produced by both routes of injection, but those following injection into the portal vein were larger and were confined to the right lobe. The lesions consisted in occlusion of the terminal branches of the portal vein with emboli containing amoebae, this being followed by periportal parenchymal degeneration with mild cellular infiltration. Small areas of local necrosis with polymorphonuclear leucocytic and round-cell infiltration developed. Abscesses of appreciable size (1 to 5 mm. in diameter) developed in 48 to 72 hours; larger abscesses appeared to be the result of infarction, rather than of the coalescence of small lesions. The hepatic lesions so produced were temporary and amoebae could not be recovered from them after 72 hours. It is concluded that *E. histolytica* can grow only for a very limited period in normal liver tissue.

In further experiments attempts were made to establish more permanent growth of *E. histolytica* in the guinea-pig liver. Chronic, persistent intestinal lesions were produced by alternating intracaecal injection of suspensions of trophozoites of *E. histolytica* with a course of treatment with " diodoquin " (di-iodohydroxyquinoline), one group of animals receiving one intracaecal injection and one course of treatment, and another two. Injection into the portal vein of 200,000 washed trophozoites was then carried out 14 days after the treatment. In both groups hepatic changes were observed as early as 4 hours after injection into the portal vein. Abscesses developed in some cases within 24 hours and large confluent lesions resulted, from which amoebae could be cultured up to 12 days after inoculation. The lesions were similar to those obtained in the animals in the first study inoculated without preliminary intestinal infection, but their advance was more rapid, progressive, and more severe. It has not been possible so far to repeat the experiment with bacteria-free cultures of *E. histolytica*, and therefore the possibility remains that associated bacteria may have influenced the progress of the lesions, but it is not thought that they were the cause of them. The results of these experiments confirm that abscesses in the liver may arise through metastasis of *E. histolytica* from intestinal lesions via the portal vein, and that chronic intestinal infection is an important factor in the production of severe hepatic lesions and of the persistence of amoebae in them.

J. L. Markson

304. **The Phagocytic Factor in Resistance to Diphtheria. I. Phagocytosis in Experimental Diphtheria. II. Phagocytic Activity of the Blood of Animals Actively Immunized against Diphtheria.** (Роль фагоцитарного фактора в невосприимчивости организма при дифтерии. Сообщение I. Фагоцитоз при дифтерийной инфекции в эксперименте. Сообщение II. Фагоцитаная активность крови животных при активной иммунизации против дифтерии)

A. P. MARISOVA. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] 24–26, No. 2, Feb., 1955.

In experiments carried out at the Rostov Institute of Epidemiology, Microbiology, and Hygiene, the scarified conjunctiva of the eyelids of 29 guinea-pigs was inoculated with one normal loopful of a 24-hour broth culture of *Corynebacterium diphtheriae* containing 2,000 million organisms per ml., either the Park-Williams No. 8 (PW8) strain or strains isolated from the throat in cases of diphtheria being used. Blood samples were taken twice before infection, again 24, 48, 72, and 96 hours after infection, and finally when the infection had subsided after 7 to 9 days. A mixture of 0·1 ml. of each sample with 0·1 ml. of a 24-hour culture of *C. diphtheriae* was incubated for 30 minutes at 37° C., smears made and stained, and the phagocytic index (number of micro-organisms ingested per 1,000 leucocytes) determined. Within 3 days of infection the phagocytic index increased 2 to 2½ times, after which it started to fall, reaching normal levels by the time the infection had subsided.

The phagocytic index was also determined 3, 6, 12, and 24 hours after infection in 10 guinea-pigs, and was found to have increased 1½ to 2 times during the first 3 hours. During the next 3 hours, however, it fell again, remaining stable for 2 days before rising, in these animals, to 3 to 10 times the normal level. In animals with a severe infection phagocytosis increased at a markedly slower rate than in those with a moderate or light infection. In general the phagocytic index rose 1½ to 2½ times higher in animals infected with freshly isolated strains than in those infected with the PW 8 strain.

[In view of the hypothesis advanced since 1946 that gravis strains of *C. diphtheriae* inhibit phagocytosis while mitis strains do not, it is a matter for regret that typing of the freshly isolated strains used in this work does not appear to have been carried out.]

In further experiments three groups of guinea-pigs were studied: (1) animals immunized by the successive subcutaneous injection at 10-day intervals of 0·5 ml. (13 units), 0·7 ml. (18·2 units), and 1·0 ml. (26 units) of diphtheria toxoid; (2) animals immunized with a vaccine prepared from cultures of the PW 8 strain of *C. diphtheriae* killed with ether and injected subcutaneously in successive doses of 1,000, 2,000, and 4,000 million organisms at 10-day intervals; (3) animals immunized by a combination of (1) and (2), each animal being given both prophylactics concurrently in the same dosage and at the same intervals into different sites.

A 6- to 12-fold increase of phagocytic activity against *C. diphtheriae* was observed in the blood after the second injection in Group 1, but it started to decrease in the majority of animals soon after the third injection. After 6 months 6 animals in this group were given a booster dose of 1 ml. of toxoid, after which a 2- to 10-fold increase in phagocytic activity was observed. In Group 2 a sharp increase in phagocytic activity was observed only after the third injection, the extent of which varied from 6-fold to 73-fold. In Group 3 a marked increase in phagocytic activity began after the first injections and reached a maximum (16- to 91-fold) after the third injection. *K. Zinnemann*

CHEMICAL PATHOLOGY

305. The Acid Precipitable Globulin (APG) Turbidity: a Convenient Guide to the Status of Serum Alpha-2 plus Beta Globulins

E. M. GREENSPAN. *Journal of the Mount Sinai Hospital* [*J. Mt Sinai Hosp.*] **21**, 279–288, Jan.–Feb., 1955. 6 figs., 12 refs.

The turbidity produced when 0·1 ml. of serum is diluted to 1 in 60 with an acetate buffer solution (0·14 ml. of glacial acetic acid and 1 ml. of 1·0 M sodium acetate per litre) of *p*H 4·42 and ionic strength 0·01 is termed acid precipitable globulin (A.P.G.) turbidity, and gives a measure of the total α_2 and β globulin content of the serum. The turbidity is measured at 650 mμ in a Coleman spectrophotometer after the diluted serum has been standing at room temperature for 30 minutes. A.P.G. turbidity is independent of thymol turbidity and of the serum concentrations of albumin, mucoprotein, and protein-bound polysaccharide. However, A.P.G. turbidity, which is expressed in units, cannot be correlated directly with the serum α_2 and β globulin concentrations as determined by paper electrophoresis, since A.P.G. turbidity values are suppressed by high concentrations of γ globulin; moreover, variations in the lipid : protein ratio in the A.P.G. samples cause different protein-staining affinity. Nevertheless, except for strongly hyperlipaemic sera, the A.P.G. turbidity values provide a satisfactory indication of gross changes in the serum content of α_2 and β globulin.

Determination of A.P.G. turbidity in samples of serum from 40 normal subjects aged 20 to 40 gave values of 4 to 8 units, the mean being 6·1 units and standard deviation 0·6 unit; the mean variation in replicate samples was 0·3 unit. In 39 samples of pathological serum the range was from 2 to 63 units. *J. E. Page*

306. The Effect of Hepato-biliary Diseases on the Serum Acid Precipitable Globulin (APG) Turbidity

E. M. GREENSPAN. *Journal of the Mount Sinai Hospital* [*J. Mt Sinai Hosp.*] **21**, 270–278, Jan.–Feb., 1955. 4 figs., 10 refs.

The diagnostic value of the serum acid-precipitable globulin (A.P.G.) turbidity test described by the author [see Abstract 305], which measures the total serum content of α_2 and β globulins, was studied in 174 patients with hepatogenous or obstructive jaundice at Mount Sinai Hospital, New York. Normal A.P.G. turbidity levels (4 to 8 units) were observed in 30 (81%) of the 37 patients with hepatitis, and low values in 22 (43%) of the 51 with portal cirrhosis; thus high values for A.P.G. turbidity occurred in less than 15% of the patients with hepatitis or portal cirrhosis. This contrasted with increased A.P.G. turbidity in 20 (95%) of the 21 patients with pancreatic or biliary carcinoma and in 66% of the 69 patients with inflammatory biliary obstruction, obstructive metastases, or metastatic hepatomegaly.

A comparison of these results with those obtained with the zinc sulphate turbidity test was then made. In the hepatitis–portal-cirrhosis group the ratio between the results was low in 75%, normal (0·6 to 1·8) in 20%, and high in 5%. In the obstructive-jaundice group of cases this ratio was high in 50%, normal in 40%, and low in 10%. The greatest differences in A.P.G. turbidity were observed between patients with portal cirrhosis and those with pancreatic or biliary carcinoma.

The author believes the A.P.G. turbidity test compares favourably with the zinc sulphate turbidity test in simplicity, and appears to be of value in the detection of abnormal patterns of globulin distribution in patients with hepato-biliary diseases. *J. E. Page*

HAEMATOLOGY

307. Papain-treated Red Cells in the Detection of Incomplete Antibodies

K. GOLDSMITH. *Lancet* [*Lancet*] **1**, 76–77, Jan. 8, 1955. 6 refs.

It has been shown that proteolytic enzymes modify erythrocytes so that they can be agglutinated in saline suspension by incomplete rhesus antibodies. In this paper from the Westminster Hospital, London, the author describes a modification of the papain technique of Kuhns and Bailey for the detection of incomplete antibodies which he has found to be both reliable and delicate.

The method is as follows. Two volumes of a papain suspension diluted with buffered saline is added to 2 tubes each containing one volume of thrice-washed,

packed Rh-positive and Rh-negative erythrocytes respectively. These cell suspensions are incubated for 30 minutes at 37° C. The cells are again washed and made up to a 5% concentration in 0·85% saline solution. In carrying out the test 0·1 ml. of each of the papainized erythrocyte suspensions, previously warmed to 37° C., is mixed with 0·1 ml. of the previously warmed serum to be tested and incubated at 37° C. for one hour. The results in the two tubes are then read macroscopically and microscopically for the presence of agglutination, care being taken not to allow the cells to cool during the reading.

In examining 3,370 samples of maternal serum this technique gave only 11 false positive and no false negative results. It is claimed that this method enhances the reactions of anti-A, anti-B, anti-M, anti-N, anti-Le^a, and anti-Le^b, but fails to detect anti-Fy^a.

[However, the pre-heating treatment plus the incubation period occupy two hours and thus give no saving of time. This method may reduce the number of false positive results which are associated with enzyme techniques, but in the abstracter's opinion the manipulations necessary do not recommend it for routine use.]

I. Dunsford

308. The Assay of Antihaemophilic-globulin Activity

R. Biggs, J. Eveling, and G. Richards. *British Journal of Haematology* [*Brit. J. Haemat.*] **1**, 20–34, Jan., 1955. 6 figs., 12 refs.

The method of assay of antihaemophilic-globulin (AHG) activity described in this paper from the Radcliffe Infirmary, Oxford, has the advantage that a reasonable estimate of this activity can be arrived at without the use of haemophilic blood. The method is based on the theory that the defect in haemophilia causes a failure in normal thromboplastin formation, the ability of the AHG preparations to form thromboplastin being measured by a modification of the thromboplastin-generation test, which is described in detail.

The results obtained with this technique were expressed graphically by plotting the clotting times against the concentration of dried ox AHG in the preparations used. A composite curve for many different preparations of AHG showed that the clotting time was proportional to AHG activity, regardless of the concentration of dried material. The scale was so arranged that one arbitrary unit of activity represented a clotting time of 17 seconds. It was later found that the test could be used only as a measure of relative activity of different preparations tested at the same time. The figures for AHG activity in samples kept in storage were very variable, but there was no tendency for the values to increase with time.

In normal plasma the average number of arbitrary AHG units was 0·28 per ml. In 9 haemophilic subjects the AHG activity never exceeded 10% of the normal. Samples of ox plasma gave an average figure of 3·5 units per ml. The experiments indicated that the ability of a sample to correct the clotting defect in haemophilic blood could be judged from this AHG-assay technique, and that both human and ox AHG disappeared rapidly from the blood of haemophilic patients. *E. G. Rees*

309. Serum Accelerator Factors and Antihemophilic Factor (AHF) in Early Phases of Clotting

J. B. Graham, R. D. Langdell, F. C. Morrison, and K. M. Brinkhous. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **87**, 45–48, Oct., 1954. 2 figs., 11 refs.

The citrate eluate of plasma adsorbed with barium sulphate contains, among other factors, the Christmas factor (PTC), Factor VII, and prothrombin. However, an eluate can be similarly prepared from the serum, which is free of prothrombin activity if the parent blood has been clotted by the previous addition of thromboplastin. Such an eluate the authors have designated the "serum accelerator factor" (S.A.). The barium sulphate eluate thus prepared was used in several ways in this study carried out at the University of North Carolina.

The addition of S.A. to haemophilic whole blood caused the clotting time to be reduced to the normal 5 to 8 minutes, but failed to alter the defective prothrombin utilization. Further addition of antihaemophilic globulin caused the clotting and prothrombin consumption to be more rapid than normal. The addition of S.A. to haemophilic plasma poor in platelets, with or without added antihaemophilic globulin, caused the clotting time to become more nearly normal, but the prothrombin consumption remained impaired. The latter was completely corrected by the addition of antihaemophilic globulin and platelets. Addition of S.A. to normal plasma containing platelets increased prothrombin consumption beyond the normal rate. It was also shown that platelets are essential to prothrombin consumption, and that antihaemophilic globulin is required in order to obtain optimum results in the prothrombin-time test.

It is evident from these results that the eluate has a marked effect on the clotting time of haemophilic blood without altering the defect in prothrombin utilization. It acts early in prothrombin conversion, reducing the latent period, but not significantly accelerating the conversion thereafter. This finding implies that assays of antihaemophilic activity on the basis of estimation of coagulation time may be misleading, especially when the serum factors have not been removed. *A. Brown*

MORBID ANATOMY AND CYTOLOGY

310. Subacute Erosive ("Peptic") Esophagitis. Histopathologic Study

E. D. Palmer. *Archives of Pathology* [*Arch. Path. (Chicago)*] **59**, 51–57, Jan., 1955. 5 figs., 17 refs.

It is pointed out that in the common non-specific form of oesophagitis (subacute erosive oesophagitis) treatment directed at the acid-peptic influence has been ineffective in preventing its complications and that the clinical findings in such cases do not support the view that acid-peptic corrosion is the primary aetiological factor. The author reviews the histopathology of the condition in the light of examination of biopsy specimens obtained at oesophagoscopy in 61 cases at the Walter Reed Army Medical Center, Washington, D.C. Evidence of disease,

consisting in diffuse infiltration with lymphocytes, plasma cells, and (sometimes) eosinophil granulocytes, fibrosis, and oedema, largely localized to the lamina propria mucosae, was found in all the cases. The epithelial layer was normal in 36 of the specimens and secondarily diseased, either by inflammatory exudate extending upwards from the lamina propria mucosae or by non-inflammatory superficial exfoliation, in the remainder. In 20 specimens the muscularis mucosae showed areas of oedema or fibrosis and cellular infiltration. In serial biopsy specimens taken from 12 patients over periods of 3 to 31 weeks no appreciable changes in the histopathological picture were observed.

The author concludes that these histopathological findings do not support the contention that "peptic" oesophagitis is caused by the corrosive action of regurgitated gastric juice, although once the mucosal vitality has been impaired, secretory products may help to remove dying tissue. *A. Ackroyd*

311. **The Pathology of Allergic Myocarditis and its Vascular Forms.** (К патологии аллергического миокардита и его васкулярной формы)
Y. L. Rapoport. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **33**, 18–28, Jan., 1955. 6 figs.

The author reviews the results of his previous investigations into the pathology of so-called idiopathic isolated [Fiedler's] myocarditis. This condition was at one time regarded as inevitably fatal, because diagnosis was usually made only post mortem. There is a progressive and malignant form, a milder form in which recovery takes place with myofibrosis, the outcome depending upon the extent and site of the sclerotic lesions, and a chronic form which is liable to recrudescences. The author considers that there is no ground for regarding the condition as a nosological entity. In his view it is a clinical variety of allergic myocarditis, and this term more accurately expresses the nature of the disease, which is that of an allergic response to infection or to other exciting agents such as drugs, physical strain, or pregnancy. Morphologically, three types can be distinguished: (1) the inflammatory infiltrative type, with foci of interstitial myocarditis in various areas and a varying degree of leucocytic infiltration; (2) the dystrophic type, characterized by more or less degenerative processes; and (3) a mixed type, combining both of the above processes.

It is with a vascular form of chronic allergic myocarditis that this article is concerned. In this form the clinical features are congestive heart failure, with hypertrophy of the heart muscle, and symptoms suggesting coronary insufficiency. Post-mortem pathological examination in 3 cases did not reveal any coronary arterial sclerosis, nor any valvular or endocardial change. The musculature of the atria and ventricles was hypertrophied, with foci of cellular infiltration with leucocytes in the more recent lesions and with histiocytes in the older ones. Periarteritis of the smaller branches of the coronary vessels was a common finding. Thrombi were frequently found in the walls of the atria and ventricles, and in some specimens necrotizing panarteritis with sclerosis and areas of haemorrhage was detected. Clinically, the symptoms were those of congestive heart failure with anginal pain, accompanied by gross enlargement of all heart cavities and hypertrophy without increase—indeed often with a distinct fall—in arterial pressure. The erythrocyte sedimentation rate and leucocyte count were moderately raised; there was no change in the differential leucocyte count. The electrocardiographic records varied much, in some cases being suggestive of coronary occlusion, in others of some degree of heart block. [The absence of eosinophilia in an alleged allergic disease is remarkable.]

The hypertrophy of the heart muscle is explained as being due to neurotrophic excitation, in accordance with the teaching of Pavlov, who first demonstrated the existence of trophic innervation of internal viscera in the centripetal nerves of the heart. In the author's own words, "it is thus possible to regard the cardiac hypertrophy, as also the consequent disturbances arising in the hypertrophied muscle and leading to its decompensation, as a single neurogenic, conditioned pathogenetic chain, the fundamental link of which is formed by the trophic impulses passing from the pressor nerve". He cites in support of his views the recently published work of Benninhof, who observed in experimentally induced hypertrophy of skeletal and intestinal muscle an increase of 25 to 30% in the size of the ganglion cells of the anterior horn of the relevant segment of the spinal cord. The author regards the allergic reaction as an expression of heightened nervous activity.

[This is an original and challenging article worthy of attention. But whether the author has sufficiently proved the allergic nature of Fiedler's myocarditis and its variants to justify a change of nomenclature at this stage is open to question. The reported absence of eosinophilia in a disease which in many ways resembles periarteritis nodosa should be confirmed by further observation.] *L. Firman-Edwards*

312. **Pulmonary Hemosiderosis in Mitral Stenosis**
H. E. Taylor and G. F. Strong. *Annals of Internal Medicine* [*Ann. intern. Med.*] **42**, 26–35, Jan., 1955. 5 figs., 10 refs.

This is a retrospective study of the morbid histology of the lungs in 45 cases of mitral stenosis occurring in a consecutive series of 3,401 necropsies performed at Vancouver General Hospital (University of British Columbia) during the 3 years 1950–2. There were, on average, 3 blocks of lung tissue available per case, and new sections were cut and examined for haemosiderosis. Marked focal haemosiderosis was present in 11 cases and mild focal haemosiderosis in a further 8. The degree of haemosiderosis found was more closely correlated with the amount of right ventricular hypertrophy present than with the degree of mitral stenosis, and on the whole its incidence was greater in patients dying before the age of 50 than in older patients. The authors agree with Lendrum *et al.* (*Quart. J. Med.*, 1950, **19**, 249 and *J. Path. Bact.*, 1950, **62**, 555; *Abstracts of World Medicine*, 1951, **9**, 146 and 592) that impregnation of the elastica, with fragmentation, is a result of the excess of

iron; they found, however, little evidence of fibrosis and no giant-cell granulomata. They consider that the aggregates of siderophages forming the nodules in this condition are the result of repeated small pulmonary haemorrhages, but do not accept the suggestion of Lendrum *et al.* that the distribution of the phagocytes can be related to haemorrhage in the alveolar ducts. They admit, however, that they cannot adequately explain the nodular distribution. *A. C. Lendrum*

313. **Pulmonary Muscular Hyperplasia (Muscular Cirrhosis of the Lungs)**
L. RUBENSTEIN, W. H. GUTSTEIN, and H. LEPOW. *Annals of Internal Medicine* [*Ann. intern. Med.*] **42**, 36–43, Jan., 1955. 3 figs., 9 refs.

Two cases are described in which hyperplasia of the smooth muscle of the lungs was found at necropsy at Lincoln Hospital, New York. Both patients died from respiratory failure due to chronic pulmonary infection, and the point is made that proliferation of muscle in the lung, when it occurs, is constantly associated with chronic inflammatory lesions of the type which more commonly results in fibrosis. The authors suggest that in such cases the degree and duration of pulmonary insufficiency have been only enough to cause a compensatory increase in muscle tissue. *A. C. Lendrum*

314. **The Pulmonary Lesions in Cryptococcosis with Special Reference to Subpleural Nodules**
R. K. HAUGEN and R. D. BAKER. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **24**, 1381–1390, Dec., 1954. 7 figs., 13 refs.

The pulmonary lesions in 12 cases of cryptococcosis are described. In contrast, the absence of pulmonary lesions at autopsy in 3 cases of cryptococcal meningitis is cited. The most common lesion at autopsy, 6 cases, was a subpleural nodule less than 1·5 cm. in diameter. This was an incidental finding at autopsy in 4 patients who died of a variety of conditions unrelated to cryptococcosis. A similar nodule was found in 2 patients in which death was due to cryptococcosis of the central nervous system. These nodules were predominantly nonencapsulated conglomerations of giant cells, lymphocytes, macrophages, occasional " caseous " necrosis, and fibrous tissue with numerous organisms. A less common lesion was a larger pulmonary nodule, from 3·5 to 7·5 cm. in diameter. These were observed in 3 surgically resected lungs, and were like the smaller nodules, except for a tendency to central necrosis and formation of a cavity. The cryptococcosis seemed to be confined to the lungs in these 3 patients. Diffuse miliary pulmonary lesions were present in 3 cases and consisted of gelatinous masses of organisms in 2 cases and micro-abscesses in 1. The miliary pulmonary lesions were a part of disseminated, systemic disease.

No large, gelatinous, lobar lesions and no large cavities were present in this series, such as those described in the literature. Calcification was not observed in any of the lesions. Accompanying involvement of hilar lymph nodes, analogous to the primary complex of tuberculosis, was not demonstrated.

Small subpleural nodules of cryptococcosis are probably more frequent than is generally suspected. They are often conglomerate masses of giant cells without limiting capsules and without great tendency to calcification, differing therein from many, but not all, tuberculomas. It is believed that (1) these nodules may give rise to cryptococcosis of the central nervous system in some patients, and then regress completely, or (2) such nodules may remain in the lung for long intervals of time in other patients, and even regress completely, without leading to cryptococcosis of the central nervous system.—[Authors' summary.]

315. **Wegener's Granulomatosis. Pathology and Review of the Literature**
G. C. GODMAN and J. CHURG. *Archives of Pathology* [*Arch. Path.* (*Chicago*)] **58**, 533–553, Dec., 1954. 14 figs., bibliography.

In this paper from Columbia University and Mount Sinai Hospital, New York, the authors discuss the pathological features of a syndrome characterized by severe destructive lesions of the respiratory tract, generalized arteritis, and necrotizing glomerulitis (Wegener's granulomatosis). They describe 7 cases in detail and summarize the findings in 22 cases reported in the literature. The ages of the patients in their series, 5 males and 2 females, ranged from 12 to 50 years, 6 being over 35. The duration of the illness before death was 2 to 5 months in 4 patients, 14 months in one, and 48 months in one; the remaining patient was alive 3 years after the onset of symptoms. At necropsy granulomata were found in the lungs, liver, spleen, kidneys, and lymph nodes. The vascular lesions were distributed as in periarteritis.

The authors consider that the pathological changes and clinical features indicate a distinct disease entity, as first recognized by Wegener. *J. B. Enticknap*

316. **Angioglomerulotubular Lipidosis without the Humoral Syndrome of Nephrosis.** (La lipidose angioglomérulo-tubulaire sans syndrome humoral de néphrose)
A. CAMELIN, J. FEROLDI, and F. BENAZET. *Presse médicale* [*Presse méd.*] **62**, 1831–1832, Dec. 25, 1954. 8 figs., 5 refs.

The authors of this very brief paper from the Lyons Faculty of Medicine advocate the study of frozen sections of the kidney stained for fat in cases of renal disease. They claim that fatty infiltration can be demonstrated in various conditions other than lipoid nephrosis, although it is usually absent in chronic nephritis and renal hypoplasia. Two illustrative cases are described, with photomicrographs: in the first, a case of malignant hypertension, the authors observed fat in the arterioles, glomeruli, and tubule cells; in the second similar appearances were found in a hypoplastic kidney which was removed along with the adrenal gland from a woman with hypertension. *A. C. Lendrum*

317. **The Selective Affinity of Anionic Detergents for Elastica: a New Stain for Elastica**
R. B. STOUGHTON. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **24**, 89–95, Feb., 1955. 2 figs., 15 refs.

Microbiology and Parasitology

VIRUSES

318. **Studies on the Cytopathogenicity of the Poliomyelitis Virus (Type Leon).** (Untersuchungen zur Cytopathogenität des Poliomyelitisvirus (Typ Leon)
W. KLÖNE. *Archiv für die gesamte Virusforschung* [*Arch. ges. Virusforsch.*] **6**, 36–44, 1955. 9 figs., 8 refs.

At the University Neurological Clinic, Hamburg–Eppendorf, phase-contrast microscopy was used to study the changes which occur in a single cell of a tissue culture of monkey kidney infected with Type-III poliomyelitis virus. The cultures were observed directly and at 37° C., the best optical conditions being obtained when clear bovine amniotic fluid was used for the fluid phase. The changes in the cell are described as follows. The first sign of infection is an increase in the prominence of the mitochondria. The nucleoli then become less compact and the nuclear membrane less distinct. As cellular shrinkage proceeds, protoplasmic threads are left behind and the nucleus may assume a peripheral position, cytoplasmic vacuoles often appearing at this stage. The final shape of the cell is ellipsoidal, with protoplasmic threads still attached. (These changes are shown in good photomicrographs.) *J. E. M. Whitehead*

319. **Virological Diagnosis of Poliomyelitis by Means of a Simplified Technique for the Propagation of the Virus in Cultures of Strain HeLa Human Epithelial Cells.** [In English]
A. KRET. *Archiv für die gesamte Virusforschung* [*Arch. ges. Virusforsch.*] **6**, 60–64, 1955. 5 refs.

Certain simplifications of the tissue-culture methods introduced at the Netherlands Institute of Preventive Medicine, Leiden, in 1953 for the cultivation of poliomyelitis virus are described. Instead of using trypsin to obtain dispersion of the epithelial cells from human carcinoma of the cervix (Strain HeLa) the clumps of cells are first centrifuged for 5 to 7 minutes at 3,000 r.p.m. and the sediment rubbed with a glass rod, the end of which has been accurately ground to a spherical shape. The cells are then resuspended in the nutritive medium, in which they form an even suspension. The nutritive medium contains, in addition to antibiotics, only 10 parts of 5% lactalbumin hydrolysate, horse serum, and Hanks's balanced salt solution.

For virus isolation a 10 to 20% faecal suspension is frozen at −20° C., thawed, and centrifuged for 15 minutes at 3,000 r.p.m. A clear supernatant results, 0·1 ml. of which is then inoculated without further treatment into each of 9 culture tubes. To overcome the toxic effect of some stool suspensions the culture fluids in the first 3 tubes are replaced after 30 minutes, the second after 4 hours, and the remainder after 24 hours. Activated carbon (5%) was also effective in removing toxicity from stools without causing appreciable loss of virus content. *J. E. M. Whitehead*

320. **Isolation of a Non-neurotropic Variant of Type I Poliomyelitis Virus**
C. P. LI and M. SCHAEFFER. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **87**, 148–153, Oct., 1954. 16 refs.

This report from the Communicable Disease Center of the U.S. Public Health Service describes the emergence of various mutants of the Mahoney strain of Type-I poliomyelitis virus during its propagation in various animal tissues. The first variant (LS) was derived from the original strain after 9 consecutive passages in monkey testicular tissue cultures. A substrain (LS-a) was derived by adaptation to mice by the intraspinal route, and this in turn provided a mouse "cerebral" strain (LS-b) after prolonged intracranial passage. Strain LS, after 33 consecutive monkey tissue culture passages (15 in testicular, 18 in kidney tissue preparations), was injected intracutaneously into a monkey and thereafter carried to tissue culture and monkey skin alternately; it continued to grow well in tissue culture, but became avirulent for mice and monkeys after the seventh monkey skin passage, this strain being designated LS-c. Preliminary evidence was obtained that this dermal variant induces a good antibody response and resists further challenge with the highly virulent Mahoney strain. The differentiation of these variants on the basis of host reactions is summarized as follows:

Strain	Tissue Culture	Monkey		Mice	
		Intra-cerebral	Intra-spinal	Intra-cerebral	Intra-spinal
Mahoney	+	+	+	−	−
LS ..	+	−	+	−	+
LS-a ..	+	−	+	−	+
LS-b ..	+	−	+	+	+
LS-c ..	+	−	−	−	−

D. Geraint James

321. **Appearances Associated with Filamentous Forms of Influenza Viruses.** [In English]
I. ARCHETTI. *Archiv für die gesamte Virusforschung* [*Arch. ges. Virusforsch.*] **6**, 29–35, 1955. 8 figs., 14 refs.

In this investigation 2 strains of influenza virus A, isolated in Rome in 1953, were used to infect the allantoic cavity of 10-day-old eggs, the allantoic fluid being collected 2 days later after chilling overnight. Preparations suitable for examination under the electron microscope were made from virus adsorbed on erythrocyte "ghosts" and fixed with osmic acid, both unshadowed and chromium-shadowed micrographs being examined. In addition to the usual filamentous forms of the virus these preparations also showed filaments which bore at their extremities spherical bodies varying from 150 to 500 mμ in diameter. In some preparations these bodies

appeared to be composed of an aggregation of smaller particles. Such bodies were not found in normal allantoic fluid or in allantoic fluid infected with strains of virus which produce mainly elementary bodies. The author considers that the presence of these large spherical bodies may indicate a different mechanism of virus release from that found in strains producing mainly elementary bodies. *J. E. M. Whitehead*

BACTERIA

322 (*a*). **Charcoal Media for the Cultivation of Tubercle Bacilli**

J. G. HIRSCH. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 955–976, Dec., 1954. 7 figs., 19 refs.

322 (*b*). **Studies of Egg-yolk Growth Factors for Tubercle Bacilli**

J. G. HIRSCH. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 977–988, Dec., 1954. 9 refs.

322 (*c*). **The Use of Charcoal in Diluents for Tubercle Bacilli**

J. G. HIRSCH. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 989–994, Dec., 1954. 9 refs.

These three papers are concerned primarily with the detoxifying effect of charcoal—particularly an activated animal preparation known as " norite A "—against substances noxious to the tubercle bacillus in the culture medium during growth of the organism, in the glassware, or in the supporting medium of living suspensions of tubercle bacilli.

In the first paper the author describes the culture of tubercle bacilli on a charcoal agar medium containing inorganic salts, glycerin, and asparagine as well as casein hydrolysate and cholesterol. The advantages of this medium are cheapness, reproducibility, and ease of preparation; in addition its growth-promoting properties are equal to those of oleic acid–albumin medium. The particular role of the charcoal in the new medium is to counter the toxic effect of agar-agar against the tubercle bacillus.

Isolation from egg yolk, after extraction with organic solvents, of a substance promoting growth of the tubercle bacillus is described in the second paper. This egg-yolk substance when added to charcoal agar enhances the growth of all strains of tubercle bacilli. Again the effect is thought to be due to the detoxification of the noxious substances in the medium.

The third paper is concerned with the protective effect of dilute suspensions of charcoal (0·01% norite A in water or phosphate buffer) on the viability of tubercle bacilli held in suspension. When tubercle bacilli are suspended in distilled water, phosphate buffer, or balanced salt solutions they rapidly lose viability on storage at room temperature in the dark, but the addition of as little as 0·01% of norite A maintains viability almost at the original level for as long as a week. The author suggests that the loss of viability of tubercle bacilli in suspension is due to the presence of antibacterial substances in the suspending medium or in the glass-ware, and that the addition of the charcoal protects the organisms and thus prolongs their viability. He further suggests that a dilute suspension of charcoal might be suitable as a stabilizer for B.C.G. vaccine.

H. J. Bensted

323. **The Cultural Characteristics and Animal Pathogenicity of an Atypical Acid-fast Organism which Causes Human Disease**

A. POLLAK and V. B. BUHLER. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **71**, 74–87, Jan., 1955. 13 figs., 10 refs.

A preliminary report of 2 cases of infection with an atypical acid-fast bacillus (" yellow bacillus ") has already been published (*Amer. J. clin. Path.*, 1953, **23**, 363). In the present paper from the University of Kansas School of Medicine and the City General Hospital, Kansas, the authors discuss the cultural characteristics of the organism and its pathogenicity for animals. This bacillus is about 3 times the length of *Mycobacterium tuberculosis* H37Rv and grows rapidly at 37° C. on all ordinary media used for routine culture of *Myco. tuberculosis*. The colonies are usually smooth and moist and the colour varies from cream to yellow.

In animal experiments the organism failed to produce progressive lesions in the guinea-pig, rabbit, or chicken. The tissue reactions in the rat and mouse were variable, but in the hamster the organism consistently caused progressive fatal disease. Administration of cortisone increased the severity of the disease in the hamster but, in the dosage used, had no effect on the other animals.

In the investigation already reported (see reference above) the bacillus was isolated from the sputum and lung tissue of a man suffering from a disease clinically resembling pulmonary tuberculosis. In the second case it was cultured from an inguinal sinus which developed after operation for the removal of a lymph node and, post mortem, from caseous lesions. All efforts to recover typical tubercle bacilli in these 2 cases by direct culture and animal inoculation failed. The pathological processes seen in the human cases are not described, but it is assumed by the authors that the organism isolated was responsible for the clinical condition.

H. J. Bensted

324. **Effects of Sunlamp Irradiation on the Viability, Virulence, and Biochemical Activity of *Mycobacterium tuberculosis***

W. SEGAL and H. BLOCH. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **71**, 112–125, Jan., 1955. 2 figs., 16 refs.

In an investigation of the effect of sunlight on the viability, virulence, and biochemical activity of *Mycobacterium tuberculosis* the authors used as a standard source of light a 100-watt sunlamp which emits radiation comparable to the ultraviolet radiation of sunlight (approximately 2,800 to 3,970 Å) in addition to visible radiation (3,970 to 7,594 Å). The various strains used were H37Rv, H37Ra, and B.C.G. " Phipps " (attenuated), and the irradiation times varied from 4 to 24 minutes.

A very marked lethal effect of irradiation was evident for all three strains. The avirulent Strain H37Ra was

the most susceptible to the germicidal effect of light and the virulent Strain H37Rv the most resistant; the attenuated B.C.G. strain was intermediate. Viability was measured by hydrogen transfer capacity tested by reduction of 2 : 3 : 5-triphenyltetrazolium chloride. It was found that virulence for mice of the H37Rv strain was much reduced by irradiation and that any given dose of radiation resulted in a greater reduction in viable counts than in the rate of respiration. Attention is drawn to the protective effect of bovine albumin (Fraction 5) on irradiation of B.C.G. suspensions, but it was noted that this protective effect was only markedly significant for short periods of exposure, being most pronounced at 4 minutes. *H. J. Bensted*

325. **An Investigation of *Neisseria gonorrhoeae* by a Red Cell Sensitization Technique**

I. CHANARIN. *Journal of Hygiene* [*J. Hyg.* (*Lond.*)] **52**, 425–443, Dec., 1954. 16 refs.

An extract prepared from freshly isolated strains of *Neisseria gonorrhoeae* was shown to sensitize sheep erythrocytes so that they were haemolysed by a homologous antiserum prepared in the rabbit. The author, working at the Central Pathological Laboratory, Durban, has investigated in detail the part played by the various components in the reaction; the techniques employed are fully described. Of the various factors concerned in the adsorption of the antigen by the erythrocytes, one was shown to be the strength, within limits, of the extract. Prolongation of the reaction beyond 30 minutes had little effect, most of the sensitization occurring within that time. In a study of the effect of different temperatures it was shown that very little adsorption occurred at 4° C., the optimum temperature being 37° C. The presence of electrolytes was necessary for the reaction. It was found that all the antigen in the solution could be adsorbed by the erythrocytes even after repeated sensitization. Strains of *N. gonorrhoeae* which had undergone the "smooth to rough" (S–R) change were no longer capable of producing a sensitizing antigen. The antigen was shown to be heat-stable and is thought to be probably polysaccharide in nature.

Initially 18 strains were examined, which by the mirror cross-absorption technique could be divided into two types, 15 being of Type I and 3 of Type II; these types share a common antigen, and Type I has an additional antigen. Examination of 67 further strains showed that 59 were of Type I and 8 of Type II, while 8 strains of meningococcus examined were found to have an antigen identical with the gonococcal Type I. Of 28 strains of other neisseria, only one showed any cross-reaction with the gonococcal antiserum. The author also demonstrated that the erythrocyte-sensitizing antigen did not fix complement, but that another antigen was present in the extract which did. The application of these findings to human infection was felt to be outside the scope of this study, but the author mentions that 30% of patients with simple gonococcal urethritis gave a positive gonococcal haemolysis test, thus suggesting that the sensitizing haptene does play some part in the process of gonococcal infection. In conclusion the author emphasizes the importance of the S–R change in any work on the antigens of *N. gonorrhoeae*.

[Recently Wilson (*J. Path. Bact.*, 1954, **68**, 495; *Abstracts of World Medicine*, 1955, **17**, 435) described experiments in which he identified 4 group antigens and 4 type-specific antigens in gonococci. He also discussed at length the S–R change and other changes in the agglutinability of the microorganism.] *R. F. Jennison*

SEROLOGY AND IMMUNOLOGY

326. **Antibody Responses of Man to Three Types of Antityphoid Immunizing Agents: Heat–Phenol Fluid Vaccine, Acetone-dehydrated Vaccine, and Isolated Vi and O Antigens**

M. LANDY, S. GAINES, J. R. SEAL, and J. E. WHITESIDE. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **44**, 1572–1579, Dec., 1954. 2 figs., 19 refs.

The authors have made a comparative study of the Vi- and O-antibody response of human subjects to 3 types of antityphoid immunizing agent: (1) a heat-killed, phenol-preserved suspension containing 1,000 million *Salmonella typhosa* (Vi strain) and 250 million each of *S. paratyphi* and *S. schottmuelleri* per ml.; (2) an acetone-killed, dehydrated vaccine which when reconstituted contained concentrations of typhoid and paratyphoid bacilli similar to the first preparation; and (3) a mixture of Vi and O antigens prepared from *Escherichia coli* and *S. typhosa* respectively. The 234 subjects were naval recruits aged 17 to 22 years, some of whom had previously had either typhoid fever or typhoid vaccine. Before immunization samples of blood were taken from all of them. The bacterial vaccines (1 and 2) were given to 74 and 57 men respectively in doses of 0·5 ml. subcutaneously at weekly intervals for 3 weeks and blood samples taken 28 and 42 days later. The purified Vi and O antigens were given to 103 men in a single dose of 0·5 ml. subcutaneously and the subjects bled 21 and 42 days later. Determination of Vi antibody was made by haemagglutination of antigen-coated erythrocyte suspensions, and that of O antibody by agglutination of alcohol-killed suspensions of *S. typhosa*.

Of those receiving Vaccine 1, 20% developed Vi antibody, with titres of 1 in 7·5 to 1 in 30; of those given Vaccine 2, 75% developed Vi antibody, with titres of 1 in 7·5 to 1 in 240; and of those given the Vi and O antigens, 100% developed antibody, with titres of 1 in 30 to 1 in 960. After all three immunizing agents all subjects developed O antibody with the following titres: (1) 1 in 20 to 1 in 1,280, (2) 1 in 20 to 1 in 320, and (3) 1 in 80 to 1 in 1,280. The reactions to the injections were moderate and varied little in the three different groups. The response of the subjects to Vi and O antigens, either in the form of vaccines or isolated products, was not modified by previous antityphoid inoculation.

The authors realize that their results do not necessarily indicate the relative protective potencies of these three preparations in man, but point out that their previous experiments on mice have shown that Vi antigenicity

and protective power run parallel. They claim that their trials represent the first employment of purified Vi and O antigens for antityphoid immunization of human subjects. *L. J. M. Laurent*

327. **The Significance of Serological Reactions in Human Toxoplasmosis.** (Sur la signification des réactions sérologiques de la toxoplasmose en clinique humaine)
M. LELONG and G. DESMONTS. *Presse médicale* [*Presse méd.*] **63**, 133–134, Feb. 2, 1955. 4 figs., 25 refs.

The authors discuss the significance of the complement-fixation test and also a modification of the dye test of Sabin and Feldman (*Science*, 1948, **108**, 660) which they have employed at the Hospital of St Vincent-de-Paul, Paris, in the diagnosis of toxoplasmosis. For the former test the complement-fixation antigen was obtained from the peritoneal exudate of infected mice. Fixation was allowed to take place for 16 hours at 4° C. and the serum was then tested for complement against a haemolytic system, as in the Kolmer test for syphilis. The dye test was modified by counting under the phase-contrast microscope the number of organisms which had undergone lysis, instead of staining them with a dye. For this reason the authors have named the modification the " lysis test ".

A total of 356 sera were examined by both techniques. Comparison of the results showed that there was a quantitative relationship between the two; for example, positive complement fixation at dilutions of more than 1 in 32 and of 1 in 4 was associated with a positive lysis-test result at dilutions of more than 1 in 500 and more than 1 in 50 respectively. In no case was the result of the complement-fixation test positive and that of the lysis test negative, although in 5 cases the former was negative and the latter positive at 1 in 100, the former becoming positive later in 3 of them. In a further case complement fixation occurred only with undiluted serum, although the result of the lysis test was positive at 1 in 2,000, but one month later complement fixation was positive at 1 in 64 and lysis at 1 in 5,000. It is stated that such cases represent recent infections in which the complement reaction is developing.

The authors then tested 20 cases of congenital toxoplasmosis in children for complement fixation. The results were positive, dilutions in the first year of life being 1 in 32 or higher; in the second year some remained high while others fell to 1 in 4. A test of 18 mothers of these children showed that in these subjects the titre fell more rapidly, and after 4 years the result was sometimes negative. It is considered that a positive test result in high dilution indicates an infection within the previous 2 years, and a weak reaction suggests an older infection, possibly up to 10 years previously. The complement-fixation test was also performed on 500 normal subjects. The incidence of positive reactions rose steadily with age to adult life, being *nil* in 144 infants, present in 18·6% of 70 children aged 2 to 5 years, in 27·4% of 73 children aged 5 to 15 years, in 37·8% of 140 subjects aged 15 to 30 years, and in 24·7% of 73 adults over 30 years of age. High titres, however, became lower with age. In the authors' opinion the rising incidence of positive reactors in childhood is best explained by the probable presence of occult infections in this age period. It is significant that of 3 adults with a titre of 1 in 16, 2 were workers in a laboratory in which infected animals are handled.

[This paper emphasizes the value of the complement-fixation test in indicating a recent infection if a rising titre is obtained. It also confirms the prevalence of *Toxoplasma* infection, as has been indicated in most recent papers on the subject. The danger to laboratory workers was recently re-emphasized by Beverley *et al.* (*Brit. med. J.*, 1955, **1**, 577).] *H. G. Farquhar*

328. **Studies on Production of Antipoliomyelitis Serum in Rabbits**
S. O. LEVINSON, A. MILZER, H. J. SHAUGNESSY, A. M. WOLF, M. JANOTA, K. VANDERBOOM, J. L. NEAL, and R. A. MORRISSEY. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol.* (*N.Y.*)] **87**, 111–114, Oct., 1954. 8 refs.

Experiments performed at the Michael Reese Hospital and Illinois Department of Public Health, Chicago, show that type-specific neutralizing antibodies to poliomyelitis virus can be produced in rabbits. The antigens used in these studies were prepared from the three types of poliomyelitis virus, propagated in cultures of monkey kidney tissue. Suspensions of both active virus and virus which had been inactivated by ultraviolet light were effective in stimulating antibody formation, although the former proved the more potent antigen. The antibody response was proportional to the amount of antigen and number of doses given, 3 intramuscular injections of 5 ml. given at weekly intervals being approximately equivalent to 7 intravenous injections of 10 ml. given twice weekly.

The antibody response to each virus type was homotypic, and in no instance was cross-neutralization observed. An irradiated vaccine containing equal quantities of all three types of virus provoked the simultaneous production of significant amounts of all three types of antibody. The possibility of using rabbits for the assay of poliomyelitis vaccine is discussed.
D. Geraint James

329. **Complement Fixation in the C-Reactive Protein System**
L. H. MUSCHEL and R. J. WEATHERWAX. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol.* (*N.Y.*)] **87**, 191–193, Oct., 1954. 11 refs.

A description is given of an improved method for the detection and estimation of C-reactive protein in which a complement-fixation technique is employed. [The details must be sought in the original paper.] Parallel estimations by this method and the usual method, which uses a precipitation reaction, showed the former to have greater sensitivity and precision. [The value of any immunological diagnostic procedure that proves positive in such a variety of clinical conditions seems problematical.] *G. Payling Wright*

Pharmacology

330. **Cardiovascular and Central Nervous System Effects of Morphinan Series**
W. SCHALLEK and D. WALZ. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **87**, 233–236, Oct., 1954. 2 figs., 9 refs.

The authors have studied the effects of five drugs of the morphinan group on the electroencephalogram (EEG), electrocardiogram, and blood pressure of dogs anaesthetized with thiopentone and immobilized with decamethonium. The morphinan drugs, levorphan tartrate, dextrorphan tartrate, levomethorphan hydrobromide, dextromethorphan hydrobromide, and levallorphan tartrate, were given intravenously in doses of 1 mg. per kg. body weight. All of them produced bradycardia and large, slow waves in the EEG—signs which were ascribed to central depression—while some had in addition a hypotensive effect which was probably due to peripheral action.

The individual effects were as follows. Levorphan produced bradycardia and marked changes in the EEG but little hypotension, dextrorphan produced marked hypotension, moderate bradycardia, but only mild EEG changes, while levomethorphan and dextromethorphan exhibited only slight central and peripheral actions. Levallorphan had little action by itself, but in further experiments was shown to be the only drug of the group which antagonized the effects of levorphan. This antagonism was most effective in animals already depressed by levorphan; simultaneous injection of the 2 drugs produced only partial antagonism, and the prior injection of levallorphan did not prevent the action of levorphan. *T. B. Begg*

331. **Probenicid (Benemid). Its Uses and Side-Effects in 2,502 Patients**
W. P. BOGER and S. C. STRICKLAND. *Archives of Internal Medicine* [*Arch. intern. Med.*] **95**, 83–92, Jan., 1955. Bibliography.

This paper from Norristown State Hospital, Pennsylvania, is mainly concerned with the side-effects of probenicid as revealed in the records of 2,502 cases in which this drug was administered, collected from the literature, from unpublished personal communications, and the authors' practice. The average daily dose tolerated was 2 g. except in patients with impaired renal function, when the dose was decreased by trial and error. In patients with gout dosage varied from 0·25 to 4·0 g. daily, and the authors found that 98 of the 2,502 patients had taken 1 to 2 g. of probenicid continuously for 1 to 4 years. Severe side-effects were rare, the most serious being hypersensitivity, with the development of chills, fever, rash, nausea, vomiting, dyspnoea, myalgia, and vasomotor collapse. There were no deaths attributable to probenicid. Skin rashes were seen in 34 patients and were usually accompanied by fever; the authors suggest that in some of the cases the rash was caused by penicillin which was given in conjunction with probenicid. Gastrointestinal symptoms, which were observed in 78 patients, included anorexia, nausea, abdominal cramps, vomiting, and diarrhoea. The uricosuric action of the drug in gouty patients caused haematuria, costovertebral pain, and renal colic, complications which can be avoided, it is suggested, by adequate alkalinization of the urine. In 10% of gouty patients acute attacks occurred in the early stages of treatment, but with continued administration of the drug these attacks appeared to be less frequent and less severe. Probenicid had no demonstrable toxic effects on the kidney and did not aggravate pre-existing kidney disease. There was no evidence of hepatic toxicity or of suppression of haematopoietic activity.

The authors conclude that probenicid is a drug of low toxicity which is valuable in chronic gout and gouty arthritis and as an adjuvant to penicillin orally or parenterally administered. *I. Ansell*

332. **Mechanism of Vasomotor Action of Veratrum Alkaloids: Extravagal Sites of Action of Veriloid, Protoveratrine, Germitrine, Neogermitrine, Germerine, Veratridine and Veratramine**
S. C. WANG, S. H. NGAI, and R. G. GROSSMAN. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **113**, 100–114, Jan., 1955. 9 figs., 24 refs.

The alkaloids of *Veratrum viride* are known to produce bradycardia and hypotension in experimental animals, most probably mediated through the vagus nerves, but there is some controversy as to the cause of the hypotension produced in bilaterally vagotomized animals. This effect has been variously attributed to a depression of the central vasomotor mechanism, to stimulation of the nodose ganglia, and to stimulation of the carotid-sinus baroceptors and carotid chemoreceptors. Since the effects may possibly differ in different animal species the authors used both cats and dogs in the study here reported from Columbia University, New York, in which small doses of various veratrum alkaloids were applied locally to the carotid-sinus region to produce changes in the arterial blood pressure, and the central vasomotor mechanism in the medulla oblongata was directly stimulated electrically to determine changes in its excitability following administration of the various alkaloids tested.

The alkaloids fell into two groups: (1) veriloid, protoveratrine, germitrine, neogermitrine, and germerine, and (2) veratridine and veratramine. Both by intravenous administration and by local application all the alkaloids caused a fall in blood pressure with the exception of veratramine, which produced no change on local application. During the hypotensive phase the carotid-sinus pressor reflex was markedly reduced or abolished by the

alkaloids in Group 1, but was only slightly reduced by the alkaloids in Group 2. The excitability of the medullary vasomotor centre was increased by all the alkaloids in Group 1, whereas veratridine and veratramine had the opposite effect.

The hypotensive effect was independent of the activity of the carotid body, and is therefore interpreted as being due to increased repetitive firing of the carotid-sinus baroceptors. Removal of the nodose ganglia did not modify the effect. Since veratridine and veratramine depressed the vasomotor centre, it is considered that in the action of these alkaloids the carotid-sinus baroceptor mechanism plays a secondary role in the production of hypotension. In chronically sympathectomized animals or those subjected to spinal section there was no appreciable change in the blood pressure, indicating that the hypotensive effect was mediated through inhibition of the sympathetic nervous system. Local application of the alkaloids showed that they had almost no direct action on the blood vessels. Repeated intra-arterial injections resulted in comparable hypotensive effects at each attempt, provided that the arterial blood pressure and the carotid-sinus pressor reflex returned to their original levels between tests.

The authors conclude that these results show that the mechanism and site of vasomotor action are different for the several veratrum alkaloids. In vagotomized animals the peripheral afferent receptors for the Group-1 alkaloids are the carotid-sinus baroceptors; these receptors are caused to discharge intensively and continuously by the alkaloids (whether injected intravenously or locally in the region of the baroceptors), thereby producing a fall in systemic blood pressure. The central action of the Group-1 alkaloids is excitatory, as was shown by the increased excitability on direct stimulation of the medullary vasomotor centre, whereas the alkaloids in Group 2 depressed this centre.

[This paper will be of considerable interest to those concerned with the study of veratrum alkaloids, and they should consult the original paper for a full description of the experimental methods employed.] *R. Wien*

333. The Clinical Evaluation of Phenylindandione as an Anticoagulant

O. R. KRUESI and F. J. SCHILLING. *New England Journal of Medicine* [*New Engl. J. Med.*] **251**, 927–931, Dec. 2, 1954. 33 refs.

The anticoagulant effect of phenylindandione (2-phenyl-1 : 3-indandione) was studied in 81 patients at St. Luke's Hospital, New York City. The drug was given by mouth in an initial dosage of 150 to 400 mg., the majority of the patients receiving 300 mg.; the maintenance dosage varied widely (25 to 300 mg.), and was based on the prothrombin time, which was determined daily in 12·5% dilute plasma. Intermittent haematuria was observed in one patient, but otherwise there were no signs of drug toxicity. In over half the cases response to the drug was rapid, the coagulation time being doubled or trebled within 48 hours. However, the response varied greatly in different patients and in the same patient during a course of treatment, possibly because some tolerance to the drug developed; in a few cases the therapeutic prothrombin level was reached only after several days. Phenylindandione was rapidly eliminated and could be given once a day. *V. J. Woolley*

334. The Effects of Methylpentynol

P. TROTTER. *Lancet* [*Lancet*] **2**, 1302–1305, Dec. 25, 1954. 4 figs., 8 refs.

In view of the widespread use of methylpentynol, particularly for dental patients, the author has investigated the effect of this drug on the speed of reaction of a group of students, noting as a preliminary that among 3,000 ambulant patients attending King's College Hospital Dental School, London, and receiving methylpentynol (" oblivon ") as a premedicant in preparation for dental extraction no undesirable effects have been observed. The series of experiments, totalling 786 in all, were designed to test (1) reaction time by means of a machine which simulated the pedals of a motor-car, and (2) speed of reaction, coordination, accuracy, and neatness by means of the McDougall–Schuster dotting machine, an apparatus which involves the cancellation by pencil of an irregular spiral of dots which are exposed briefly on a revolving turntable.

After receiving 500 mg. of methylpentynol in two capsules by mouth the students were more confident during the tests and in discussions with their lecturer; subjective effects began in 10 to 15 minutes and lasted about one hour. The performance of the subjects in the two tests was not impaired and in a number of cases was slightly improved. After receiving ethyl alcohol in the form of 8 to 16 drachms (28 to 56 ml.) of whisky, approximately equivalent to 12·8 to 25·6 ml. of ethyl alcohol, they felt less elated and more " on guard "; it was also noted that they were unduly optimistic regarding their performance in the tests, thus confirming the views often expressed by motorists under the influence of alcohol. In fact, their performance after the consumption of ethyl alcohol was less good.

The author concludes that methylpentynol in a dose of 500 mg. has no deleterious effect on behaviour, and that not only the speed of reaction but also concentration and coordination are unimpaired or even enhanced by methylpentynol. Its effects differ markedly from those induced by ethyl alcohol. *T. B. Begg*

335. Enhancement of the Action of Certain Analgesic Drugs by β-Diethylaminoethyldiphenylpropylacetate Hydrochloride

L. COOK, G. NAVIS, and E. J. FELLOWS. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **112**, 473–479, Dec., 1954. 5 figs., 10 refs.

The authors have already shown that β-diethylaminoethyldiphenylpropylacetate hydrochloride (" SKF 525-A ") prolongs the duration of hypnosis induced by barbiturates. In a further series of experiments they found that SKF 525-A enhanced the analgesic properties of morphine, codeine, " methadone " (amidone), pethidine, and DL-methorphinan in rats, as measured by the " tail flick " method, but that the compound when given alone in the same dosage had no analgesic activity. The

respiratory depressant action of morphine and the LD_{50} of morphine and pethidine were unaffected by SKF 525-A.
B. Isaacs

336. **A Study of the Effects of Valmid, a Non-barbiturate Central Nervous System Depressant, in Humans**
C. M. GRUBER, K. G. KOHLSTAEDT, R. B. MOORE, and F. B. PECK. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **112**, 480–483, Dec., 1954. 4 refs.

A study of the sedative and hypnotic properties of "valmid" (ethinamate), a *cyclo*hexane derivative and depressant of the central nervous system, is reported. In a dosage of 0·4 to 1·2 g. ethinamate proved superior to a placebo as a nocturnal hypnotic in 6 patients. The sedation produced when 1·5 g. was given was somewhat less in degree and duration than that produced by 0·3 g. of quinalbarbitone. No significant effect on pulse rate, respiration, and blood pressure was noted with this dose of ethinamate.
B. Isaacs

337. **Inhibition of Cerebrospinal Fluid Formation by a Carbonic Anhydrase Inhibitor, 2-Acetylamino-1 : 3 : 4-thiadiazole-5-sulfonamide (Diamox)**
R. D. TSCHIRGI, R. W. FROST, and J. L. TAYLOR. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **87**, 373–376, Nov., 1954. 2 figs., 13 refs.

In view of the reported effect of 2-acetylamino-1:3:4-thiadiazole-5-sulphonamide ("diamox") on the formation of intraocular fluid, and the similarity between this fluid and cerebrospinal fluid (C.S.F.), the authors have investigated, at the University of California, Los Angeles, the effect of diamox on intracranial pressure and formation of C.F.S. The flow of C.S.F. in cats and rabbits lightly anaesthetized with pentobarbitone sodium was measured by recording the rate at which the fluid dripped from a 22-gauge spinal needle inserted in the cisterna magna. In some of the animals intracisternal pressure was measured by means of a pressure transducer. All animals were given artificial respiration, since tubocurarine was given throughout each experiment in sufficient quantities to inhibit spontaneous respiration.

After an initial equilibration period, the flow of C.S.F. and intracisternal pressure became constant. The intravenous injection of 150 mg. of diamox per kg. body weight then caused a fall in intracisternal pressure and in the C.S.F. flow-rate which continued over a period of 1 hour, when a new steady state was reached which persisted until the experiments were terminated 2 hours later. At this time the formation of C.S.F. had decreased 3- to 15-fold, with a resultant reduction in intracranial pressure of some 30%. There was no significant change in blood pressure throughout these experiments, nor was there any change in the sodium, potassium, or calcium concentration in the C.S.F. When ventilation of the animals was changed from 100% oxygen to 70% oxygen and 30% carbon dioxide there was a transient rise in the C.S.F. flow-rate and in intracisternal pressure. When the gas mixture was changed back to pure oxygen the flow-rate and the intracisternal pressure fell precipitously, but rapidly returned to the original steady state. After the administration of diamox the same procedure produced the same effects. The results are discussed and a hypothesis is presented in which it is suggested that the effect of diamox is due to its inhibition of carbonic anhydrase (known to be present in appreciable amounts in the central nervous system) brought about by alteration in the diffusion rates of hydrogen and bicarbonate ions by the blood–brain barrier.

[Since diamox also causes diuresis, a comparison of its effects in this respect with those of a simple diuretic on the C.S.F. flow-rate and intracisternal pressure would have been useful.]
P. A. Nasmyth

338. **Acetazoleamide (Diamox) Diuresis**
A. RUSKIN. *Archives of Internal Medicine* [*Arch. intern. Med.*] **95**, 24–32, Jan., 1955. 16 refs.

Working at the University of Texas, Galveston, Texas, the author has studied the diuretic effect of acetazoleamide ("diamox") when given orally to patients with and without heart failure in doses ranging from 500 mg. to 6 g. in 24 hours. With large doses the urinary volume was more than doubled in 24 hours, accompanied by a marked rise in sodium and potassium excretion. The diuresis lessened on the following day, but electrolyte excretion continued in large amounts. In some cases diuresis and weight loss continued for periods up to 3 weeks without further administration of diuretics. Toxic effects were mild paraesthesiae, drowsiness, nausea, vomiting (in 3 out of 15 cases), and the occurrence of a reversible psychosis in one patient with nephrosclerosis and uraemia. In 12 patients with heart failure receiving either a single dose or repeated dosage (500 mg. of diamox at 8-hourly intervals for 4 doses) diuresis was only slightly more effective in the second and third 8-hour periods, but with repeated dosage sodium excretion was more effective during the 24 hours and the following day than with the single dose.

Renal clearance tests, carried out with mannitol and PAH on 6 patients with heart disease and 5 without, showed inconsequential falls. The urinary volume and sodium excretion rose more markedly in the cardiac patients than in the others, and was without relation to any changes in renal haemodynamics. Ballistocardiographic studies following the injection of 250 mg. of acetazoleamide intravenously revealed no effect on the stroke volume of non-cardiac subjects, but there was generally an increase in patients with congestive failure. There was no evidence of inhibition of the activity of succinic dehydrogenase and adenosine triphosphatase in the heart and kidney. Acetazoleamide diuresis is attributed to the inhibition of carbonic anhydrase in the renal tubules, producing an alkaline urine and excessive distal tubular excretion of potassium, with a decreased tubular reabsorption of sodium, bicarbonate, and consequently of water.
I. Ansell

339. **Histamine Release and the "Stress" Phenomenon**
P. A. NASMYTH. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **10**, 51–55, March, 1955. 2 figs., 14 refs.

Chemotherapy

340. **Infections Occurring during Chemotherapy. A Study of Their Frequency, Type and Predisposing Factors**
L. WEINSTEIN, M. GOLDFIELD, and TE-WEN CHANG. *New England Journal of Medicine* [*New Engl. J. Med.*] **251**, 247–255, Aug. 12, 1954. Bibliography.

The incidence during chemotherapy of serious infections superimposed on that for which treatment was initially instituted was studied from the records of patients admitted to the Haynes Memorial Hospital, Boston, between 1946 and 1953. A total of 3,095 patients received antibiotics, and in 68 (2·19%) of these there was evidence of a superimposed infection. The disease condition for which antibiotics were originally given varied widely, but a high proportion of the patients suffered from infections of the respiratory tract. Thus 1,202 patients had pharyngitis and a further 586 had miscellaneous respiratory infections, including pneumonia (369). A complicating or superimposed infection was assumed to have developed when the primary condition responded both clinically and bacteriologically to the administration of an antibiotic but signs of active infection returned while the drug was still being given.

It was found that superimposed infection was three times more frequent in children under 3 years of age that in those aged 4 years or more. The percentage incidence (1·46) of secondary infection was lowest with penicillin therapy, rising to 7·4 with chlortetracycline. Most of these complications occurred between the third and sixth days of treatment. In general the organ involved in the secondary infection was the same as that affected initially, the respiratory tract being the commonest. *T. Anderson*

ANTIBIOTICS

341. **Therapeutic Effect of Chlortetracycline and Oxytetracycline in Immunized Mice Treated with Cortisone**
E. J. FOLEY. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **5**, 1–5, Jan., 1955. 11 refs.

Cortisone in large doses not only impairs the defences of animals to infection, but also interferes with the protective effect against such infections in non-immunized animals of certain antibiotics, including aureomycin (chlortetracyline) and oxytetracycline, suggesting that they depend for their chemotherapeutic effect on the defence mechanisms of the host. Experiments were therefore carried out to determine whether these drugs would protect immunized animals in similar circumstances. Mice were immunized against a virulent strain of *Streptococcus zooepidemicus*, Group C, by the subcutaneous injection of 0·05 ml. of an undiluted 24-hour culture followed by a fortnight's treatment with 1,000 units of penicillin or 1 mg. of aureomycin per ml. of drinking water. Those mice which showed progression of the local lesions (subcutaneous swellings or enlarged lymph nodes) or which appeared sick were rejected, the remainder being used for experiments starting 2 to 3 weeks after completion of treatment.

Groups of normal and immunized mice were infected by the intraperitoneal or intramuscular injection of 0·1 ml. of streptococcal culture and treated with aureomycin (1 to 2 mg.), oxytetracycline (2 mg.), or penicillin (1 mg.) daily in two doses starting 2 hours after infection. Other groups were treated similarly, with the addition of 0·8 mg. of cortisone daily, starting one hour after infection. Treatment was continued for 3 days. Whereas the therapeutic effectiveness of penicillin was not impaired by cortisone in either normal or immunized mice, the protective effect of aureomycin and oxytetracycline was abolished by cortisone in normal mice. Immunized mice, however, were protected by oxytetracycline and aureomycin in spite of treatment with cortisone. The relationship between the action of these antibiotics and the defence mechanisms of the host is briefly discussed. *Norval Taylor*

342. **The Antibiogram as a Means of Demonstrating Bacterial Antagonism.** (L'antibiogramme révélateur d'antagonisme bactérien)
E. DE LAVERGNE, J. C. BURDIN, and J. BEUREY. *Presse médicale* [*Presse méd.*] **62**, 1786, Dec. 25, 1954. 5 figs.

On the basis of studies carried out at the bacteriological laboratories of the Faculty of Medicine, Nancy, the authors suggest that the vigorous growth on culture-medium plates of one component of a mixture of bacteria (contained, for example, in pus or exudate), around paper disks containing an antibiotic to which it alone, of all the organisms in the mixture, is insensitive, is due to release of the insensitive organism from the antagonistic effect of the other bacteria. Colour photographs of culture plates showing this phenomenon with various organisms are reproduced. *C. L. Oakley*

343. **Penicillin by Mouth in Infancy. A Comparison between Benzathine and Sodium Penicillins**
B. LAURANCE. *British Medical Journal* [*Brit. med. J.*] **2**, 1392–1394, Dec. 11, 1954. 3 figs., 15 refs.

Benzathine penicillin or sodium penicillin was given by mouth to 20 healthy infants selected at random from two nurseries in the Bristol Maternity Hospital, and the effects of the two forms of penicillin were compared. All the infants were under 12 days old and over 5½ lb. (2·5 kg.) in weight, the average weight being 7 lb. 7½ oz. (3·4 kg.).

It was found that the blood penicillin level reached a peak 2 hours after a single dose of 150,000 units of sodium penicillin and 6 hours after a similar dose of benzathine penicillin. One group of infants received

4 doses, each of 150,000 units, of sodium penicillin at 8-hourly intervals and another group received a similar dosage of benzathine penicillin. The serum levels of the antibiotics were approximately the same 8 and 10 hours after the last dose. Adequate concentrations were obtained with both preparations. There was no evidence of a cumulative effect with benzathine penicillin.

T. Anderson

344. **The Influence of Penicillin on *Corynebacterium diphtheriae* in Experimental Diphtheria.** (Влияние пенициллина на B. diphtheriae в условиях экспериментальной дифтерийной инфекции)
E. P. KUSINA. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] **26**, No. 2, Feb., 1955.

At the Saratov Medical Institute the conjunctiva of both eyes was infected with virulent cultures of *Corynebacterium diphtheriae* in a number of guinea-pigs and penicillin was applied 1, 3, and 6 hours later to one eye only, the other eye of each animal serving as an untreated control. Results were assessed by means of microscopical and cultural examination of the secretions in addition to clinical observation.

Penicillin proved to be completely effective under these conditions. Although the shorter the period between the infection and the application of penicillin, the better was the clinical appearance of the lesion, sterility was obtained in all cases within 2 days.

Following the application of penicillin a sharp increase in the leucocytic reaction set in very rapidly, leading to complete disappearance of all macroscopic and microscopic inflammatory changes. *K. Zinnemann*

345. ***In vitro* Activity of Chloramphenicol on *Salmonella typhi***
K. C. WATSON. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **45**, 97–101, Jan., 1955. 1 fig., 12 refs.

CHEMOTHERAPY OF TUBERCULOSIS

346. ***In vitro* Study of Antitubercular Substances from *Allium* Species. Part I. *Allium schoenoprasum*. Part II. *Allium cepa***
K. C. GUPTA and R. VISWANATHAN. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **5**, 18–21, Jan., 1955. 5 refs.

Allium schoenoprasum is cultivated extensively for food in Kashmir, and *Allium cepa* throughout India. The authors report, from the University of Delhi, the extraction of substances from these plants which were shown to possess tuberculostatic activity.

The active principle of *Allium schoenoprasum* was obtained from the bulbs by two methods—steam distillation and extraction of the distillate with ether, and extraction of the crushed bulbs with alcohol and chloroform. In each case after evaporation of the vehicle an oil with a characteristic odour was left behind. This substance was added in various concentrations to nutrient broth (*p*H 7·2) which was then inoculated with a 5-mm. loopful of a 24-hour broth culture of various organisms and incubated for 18 hours at 37° C. In a concentration of 200 μg. per ml. the substance was ineffective against *Escherichia coli*, *Salmonella typhosa*, *Vibrio comma*, *Klebsiella pneumoniae*, and *Proteus vulgaris in vitro*, but had some effect on *Staphylococcus aureus*. Antituberculous activity of the drug was determined against various strains of *Mycobacterium tuberculosis* in cultures on Youman's medium, which was incubated at 37° C. for 14 days. The oil inhibited the growth of streptomycin-sensitive human strains in a concentration of 2·5 μg. per ml. and of a streptomycin-resistant strain in a concentration of 1·25 μg. per ml. Bovine and avian strains were completely inhibited by 5 μg. per ml. This substance was slightly less active than streptomycin against sensitive strains *in vitro*.

The active principle of *Allium cepa* was extracted by the same and two other methods, and inhibited the growth of tubercle bacilli *in vitro* in concentrations varying from 8 to 25 μg. per ml. The material from *Allium cepa* was about five times less active than streptomycin against streptomycin-sensitive strains.

Norval Taylor

347. **A Short Note on Antitubercular Substance from *Occium sanctum***
K. C. GUPTA and R. VISWANATHAN. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **5**, 22–23, Jan., 1955. 1 ref.

Occium sanctum, commonly known as *tulsi*, is used in Hindu medicine for the treatment of various ailments of the respiratory tract and skin diseases. Working at the University of Delhi, the authors have isolated an active substance from this plant by steam distillation and extraction with ether, and have tested its antibacterial properties by methods described by Gupta and Chopra (*Indian J. med. Res.*, 1953, **41**, 427).

The substance was found to inhibit the growth of a human strain of *Mycobacterium tuberculosis* and of *Staphylococcus aureus in vitro* in a concentration of 10 μg. per ml. Its tuberculostatic activity was 10 times less than that of streptomycin, but in comparison with isoniazid it varied according to the number of days of incubation. If the tubes were incubated for 4 to 6 days, the activity of the extract was 5 times greater than that of isoniazid; but if the tubes were incubated for 8 to 14 days, its activity became 4 times less.

Norval Taylor

348. **Combined Action of Streptomycin and Chloramphenicol with Plant Antibiotics against Tubercle Bacilli. Part I. Streptomycin and Chloramphenicol with Cepharanthine. Part II. Streptomycin and Allicin**
K. C. GUPTA and R. VISWANATHAN. *Antibiotics and Chemotherapy* (*Antibiot. and Chemother.*] **5**, 24–27, Jan., 1955. 10 refs.

The activity against the tubercle bacillus *in vitro* of streptomycin and chloramphenicol in combination with two antibiotics derived from plants was studied at the University of Delhi. The minimum concentration of streptomycin, used alone, which inhibited the growth of

Mycobacterium tuberculosis Strain H52 was 0·6 μg. per ml., and that of cepharanthine (an alkaloid from *Stephania cepharantha*), used alone, was 2 μg. per ml. When the two drugs were used together, however, growth was inhibited by only 0·1 μg. of streptomycin per ml. with 0·6 μg. of cepharanthine per ml. The minimum inhibitory concentration of chloramphenicol was 1·0 μg. per ml. and of cepharanthine 0·5 μg. per ml. when used individually against a bovine strain of tubercle bacillus (B19-3), but when used in combination 0·01 μg. of cepharanthine and 0·6 μg. of chloramphenicol per ml. were effective.

Against an unspecified strain of tubercle bacillus streptomycin used alone inhibited growth completely in a concentration of 1·6 μg. per ml. and partially in a concentration of 0·4 μg. per ml., while allicin (derived from *Allium sativum*) inhibited growth in a concentration of 10 μg. per ml. In combination, 0·8 μg. of streptomycin and 0·5 μg. of allicin per ml. inhibited the growth of the same strain completely.

Norval Taylor

349. **The PAS Content of Collapsed Lungs and Other Organs in Experimental Tuberculosis.** (Содержание ПАСК в коллабированном легком и других органах при экспериментальном туберкулезе)
A. M. Кнома. *Бюллетень экспериментальной Биологии и Медицины* [*Byull. eksper. Biol. Med.*] **39**, 46–47, Jan., 1955. 1 fig.

The concentration of PAS in the lung tissue and other organs of four groups of rabbits was determined by the colorimetric method of Ragatz [no reference given]. The 48 animals were divided as follows: (1) healthy controls, (2) healthy animals with unilateral pneumothorax, (3) animals experimentally infected with tuberculosis, and (4) tuberculous animals which had been subjected to unilateral pneumothorax. It was found that the concentration of PAS in the collapsed lungs of both healthy and infected animals (Groups 2 and 4) was significantly higher than that in normally expanded lungs (Groups 1 and 3). The concentration in the blood, liver, and kidneys of infected animals was slightly higher than in those of healthy rabbits. *A. Swan*

350. **Experimental Studies of the Bactericidal Properties of Antibacterial Agents. Clinical Trials.** (Recherches expérimentales sur le pouvoir bactéricide des agents antibacillaires. Essais cliniques)
E. Bernard, B. Kreis, and H. Lutier. *Revue de la tuberculose* [*Rev. Tuberc. (Paris)*] **18**, 1009–1028, 1954. 6 figs., 9 refs.

The authors believe that antituberculous drugs are rarely bactericidal *in vivo* but act mainly as bacteriostatics. Having shown that streptomycin, isoniazid, and high concentrations of PAS were bactericidal to *Mycobacterium tuberculosis* in plate cultures, they carried out a series of experiments which showed that plasma from 82 tuberculous patients treated with varying doses of these drugs was also bactericidal to an extent varying with the dose of the drug, some 70 to 90% of the organisms being killed when exposed for 24 hours to the plasma containing streptomycin or isoniazid; PAS alone was ineffective, but it considerably increased the effect of the other two drugs when given in combination with them.

In further experiments attempts were made to maintain a high blood level of the drugs in guinea-pigs freshly infected with tubercle bacilli, but the animals were not cured and considerable toxicity was observed. Supposedly bactericidal doses were then given in cases of established infection in guinea-pigs, mice, and human patients. To the patients maximum doses were given for 6 to 12 days and repeated at monthly intervals, but no beneficial effect could be shown. The authors regretfully conclude that however attractive the idea of bactericide by means of massive doses may be, these experiments show, for the present at least, that such treatment is less effective than regular, prolonged treatment at lower dosage as in current practice.

F. W. Chattaway

CHEMOTHERAPY OF TUMOURS

351. **"Sanamycin" (Actinomycin C) in the Treatment of Malignant Tumours and Hodgkin's Disease.** (Sanamycin (Actinomycin C) in der Behandlung bösartiger Geschwülste und der Lymphogranulomatose)
H. Schmidt, H. Loosen, and W. Heinen. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **80**, 140–143, Jan. 28, 1955. 2 figs., 19 refs.

At the University Medical Clinic, Cologne, "sanamycin" (actinomycin C, HBF-386) given by intravenous injection was used in the treatment of 30 patients suffering from Hodgkin's disease and other malignant tumours, but of these only 20 have been followed up long enough for assessment of results. Patients at all stages of the disease were treated, and all had been previously shown to be resistant to other forms of therapy. Of the 8 patients suffering from Hodgkin's disease, almost all showed definite subjective improvement, but only 4 showed objective improvement, while of the 12 cases of other diseases there was marked subjective improvement in all, but definite objective improvement in only 2.

Of particular interest was the case of a woman of 47 who had undergone nephrectomy for a hypernephroma in 1951. Following this the patient felt well for over a year, but in the autumn of 1952 there was a general decline in well-being, with loss of weight, increase of blood pressure, progressive anaemia, and radiological evidence of metastases in the lung. Despite the terminal picture and the extreme cachexia, treatment with sanamycin was begun in early 1953. At first there was subjective improvement, although the pulmonary metastases increased in size. In September, 1953, radiography showed massive infiltration in both lungs, but later that month and in early October a most unexpected improvement occurred and in radiographs taken in November, 1953, a pronounced recession of the metastases could be observed. By this time 18,000 μg. of sanamycin had been given. Increasing clinical improvement ran parallel with the *x*-ray findings. By May,

1954, the metastases were no longer visible radiologically, the patient's weight had increased by 15 kg., and the blood pressure and blood picture were almost normal.

In this series of cases sanamycin was at first given in doses of 50 to 100 μg. per day, but later doses up to 400 μg. daily were given, in some cases for several weeks, and were equally well tolerated. However, as there appeared to be no obvious advantage in high dosage a standard dose of 200 μg. daily was chosen. (Other workers have given high doses by continuous intravenous drip). Side-effects were rare and mostly mild, irritation of the mucous membrane of the mouth, throat, and stomach being noted in some cases. Reactions were severe in only 3 cases; one patient, after a total dose of 20,000 μg., developed a swelling of the mucous membrane of the throat and complained of burning in the oesophagus, while another, after receiving a total of 15,000 μg., developed gastritis, with vomiting and pain; in both these cases there was no further trouble after a temporary discontinuance of the injections. The third patient developed gastritis after the first dose, with continuous vomiting which recurred on subsequent re-administration of sanamycin. The authors consider that their results justify further trials of the drug.

Robert Hodgkinson

352. **Organ-specific Chemotherapy of Carcinoma of the Prostate.** (Organspezifische Chemotherapie des Prostata-Karzinoms)
R. BUDNIOK, H. G. STOLL, and G. ALTVATER. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **80**, 143–146, Jan. 28, 1955. 18 refs.

The authors describe the results obtained with "honvan" (ST 52-ASTA; diethyldioxystilboestrol), a new synthetic oestrogen which can be given in high intravenous dosage without severe side-effects and which has a particular affinity for carcinomatous prostatic tissue, in the treatment at St. Hedwig's Hospital, Berlin, of 209 patients suffering from carcinoma of the prostate gland during the last 2 years. There was no selection of the patients, whose average age was 68·9 years. Only about half could state the duration of the disease, and the average for these was 21·6 months, while the average duration of previous treatment was 14·6 months.

In 90% of the cases there was marked clinical improvement following treatment; 4% showed no change, and 6% were worse. In those showing improvement, difficulty in micturition was relieved and the primary tumour diminished in size. Relief from pain due to metastases was so great that in the authors' opinion the preparation can be described as a "specific analgesic", patients who could scarcely walk because of pain being able to move freely after only 5 days' treatment. It was impossible to substantiate the statement made by other workers that bone metastases decrease in size, but a reduction was certainly observed in the size of metastases occurring elsewhere. Distressing feminizing changes did not occur, but it is thought this may have been because of the high average age of the patients. There was a decrease in libido and a moderate hyperplasia of the breast tissue, which persisted for 2 to 3 months after stopping treatment. A fixed dosage schedule was not used, but in most cases 500 mg. was given daily for 10 days, followed by two injections per week of 500 mg. each. If the serum acid-phosphatase level was not then normal another 10 daily injections were given. After this period maintenance therapy depended on the serum phosphatase level. Even when this became normal it was not considered advisable to reduce the quantity below the amount given in the first 2 weeks. The importance of not discontinuing treatment too soon is stressed.

Robert Hodgkinson

353. **Experimental and Clinical Studies of a Colchicine Derivative with Antiblastic Properties: the Methyl Ester of Trimethylcolchicinic Acid (Deacetylcolchicine).** (Ricerche sperimentali e prime applicazioni cliniche con un derivato colchicinico ad azione antiblastica: l'estere metilico dell'acido trimetilcolchicinico (deacetilcolchicina))
W. PAOLINO, G. PIERRI, and L. RESEGOTTI. *Minerva medica* [*Minerva med. (Torino)*] **1**, 1–12, Jan. 6, 1955. 16 figs., 11 refs.

The activity of the methyl ester of trimethylcolchicinic acid (deacetylcholchicine) was first tested on mice, rats, and rabbits at the Institute of Special Pathology, Turin. The derivative was shown to have about one-third of the activity of colchicine in causing mitotic arrest, but no lasting effects on the blood count, the hair, or digestive tract were observed.

The ester was then subjected to clinical trial on 6 cases of myeloid leukaemia, 15 cases of Hodgkin's disease, and 16 cases of other malignant tumours. Daily doses, in most cases of 10 mg., were given until the leucocyte count had fallen. In the cases of myeloid leukaemia remissions lasting up to one month occurred and could be obtained repeatedly by further series of doses. In the cases of Hodgkin's disease improvement was observed for periods up to 20 days and was also repeatable on further dosage. In the other cases the effects were variable, but in most resulted in some slight improvement.

G. Calcutt

354. **The Action of Deacetylcolchicine on Cultures of Fibroblasts *in vitro*.** (Azione della deacetilcolchicina su culture di fibroblasti *in vitro*)
G. LENTI, E. TORTAROLO, G. VAGLIO, P. ZAINA, and G. MUSOLINO. *Minerva medica* [*Minerva med. (Torino)*] **1**, 13–18, Jan. 6, 1955. 11 figs., 17 refs.

At the Institute of Special Pathology, University of Turin, the authors have studied the action of the methyl ester of trimethylcolchicinic acid (deacetylcolchicine) on fibroblasts of the chicken heart in tissue cultures *in vitro*. Concentrations of the ester of between 0·004 mg. and 4 mg. per litre were found effective in causing arrest of maturation at the metaphasic, or premetaphasic stage, producing rounding and loss of adhesion of the cells, this being followed by accumulation of fat and eventual degeneration. The extent of these changes was directly correlated with the degree of concentration of deacetylcolchicine.

G. Calcutt

Infectious Diseases

355. **Intermittent Positive-pressure Respiration in Bulbospinal Poliomyelitis. Use of the Radcliffe Respiration Pump**

J. R. HARRIES and W. E. LAWES. *British Medical Journal* [*Brit. med. J.*] **1**, 448–454, Feb. 19, 1955. 1 fig., 22 refs.

The treatment of 3 cases of bulbospinal poliomyelitis, which included tracheotomy and intermittent positive-pressure (I.P.P.) respiration by means of a Radcliffe pump, is described. The patients were treated in the special poliomyelitis unit of the Infectious Diseases Hospital, Nairobi.

The first patient, a European air pilot aged 33 years, complained of headache and malaise for 5 days, followed by weakness of the flexors of the right hip. He was flown to hospital from Mweiga—a distance of 300 miles (480 km.)—and 24 hours after admission was placed in a tank respirator; 36 hours later tracheotomy became necessary because of pharyngeal pooling. After 17 days, attempts at replacing the I.P.P. respirator by Bragg–Paul and cuirass apparatus had to be abandoned because of episodes of hypertension and a fall in the pulse rate. At the end of the eighth week the patient was flown to England in a pressurized plane. He stood the journey well and was reported to be progressing satisfactorily.

The second patient, a male Chinese aged 46 years living in Musoma, Tanganyika, had fever, headache, and a sore throat, followed by paralysis of the left leg. Within 24 hours the right leg became paralysed also. Three days later still he developed difficulty in swallowing and was transferred by plane to Nairobi—a distance of 400 miles (640 km.). Tracheotomy and I.P.P. respiration were found to be necessary 24 hours after admission, but in spite of these measures the patient's condition continued to deteriorate, with pyrexia, hypotension, and pulmonary oedema associated with restlessness and considerable bronchial secretion. At various times paraldehyde, chlorpromazine, and a noradrenaline drip were given, but the patient died 25 days after the onset. Necropsy was not performed.

The third patient, a male European aged 40 years, was admitted to hospital in Kitale with respiratory weakness. Signs of bulbar involvement quickly developed and tracheotomy was performed and I.P.P. respiration instituted. The next day the patient was flown 300 miles to Nairobi at a height of 9,000 to 11,000 feet (2,700 to 3,350 m.). Further treatment, which included administration of chlorpromazine and bronchoscopy, was unsuccessful, and the patient died in hyperpyrexia—temperature 107° F. (41·7° C.)—36 hours after the onset. Necropsy showed the usual changes of poliomyelitis in the cord, medulla, and pons.

In all 3 cases there were mental distress and continued pyrexia. Chlorpromazine was given as a sedative and antipyretic, but this did not appear to have any effect on the temperature " unless ice and a breeze from a fan were used in addition ". The authors emphasize that even with trained medical and nursing staff and I.P.P. respiration the mortality from bulbospinal poliomyelitis is high when such complications as shock, hyperpyrexia, and pulmonary oedema develop.

[This report is interesting because it shows that air transport of serious cases of bulbospinal poliomyelitis is practicable. It may nevertheless be inadvisable to move these very ill patients such long distances in the acute stage, because the strain of the journey may contribute to a spread of damage within the central nervous system. Other points brought out in this paper are: (1) hot climate makes treatment difficult, especially control of the patient's temperature; (2) the dangers of mental distress and the need for continued encouragement of the patient; (3) the risks of over-treatment, an understanding of which, in the abstracter's view, is important in the management of these cases; and (4) the prognosis in severe cases depends not so much on the local danger of pharyngeal pooling, as on the extent of the damage inflicted on the medulla by the virus.]

I. M. Librach

356. **Problems Involved in Prevention of Bacterial Complications of Measles, with Special Reference to Prophylactic Sulphadiazine**

G. I. WATSON. *British Medical Journal* [*Brit. med. J.*] **1**, 5–10, Jan. 1, 1955. 11 refs.

The author, a general practitioner, has attempted to assess the effect upon the bacterial complications of measles of prophylactic administration of sulphadiazine. Of 142 patients with measles seen during an epidemic, 90 received sulphadiazine prophylactically. The patients selected were under 3 years of age or regarded as " poor risks "—that is, there was evidence of bacterial infection when the patient was first seen early in the disease or a history of previous respiratory infection—the so-called catarrhal patient. The material on which the author bases his conclusions is analysed in 13 tables. He states that when sulphadiazine was given in " near-curative doses to children, especially catarrhal children who showed signs of active bacterial infection at the start of their measles, the drug reduced the severity of the bacterial infection in about half the treated cases, while the remainder had probably received an insufficient dosage ". On the other hand, when the drug was given to " normal children apparently free of bacterial infection at the start of their measles, it appeared to confer no benefit, but rather to increase the rate and severity of complications as compared with similar untreated children ". [It is not clear that the latter conclusion is soundly based. Tests for statistical significance of the figures given might possibly have revealed that this result could come about by chance.] The author concludes from his figures that sulphonamides are of value in some

children but not in others in the prevention of bacterial complications of measles, and suggests that this may in some way be associated with the leucopenia of the disease.

[This painstaking work, though praiseworthy in its aim of bringing precision to the subject of chemoprophylaxis in measles, seems to beg more questions than it answers.] *H. Stanley Banks*

357. **Lymphocytic Choriomeningitis in the Newborn. Probable Transplacental Infection**
G. M. KOMROWER, B. L. WILLIAMS, and P. B. STONES. *Lancet* [*Lancet*] **1**, 697–698, April 2, 1955. 9 refs.

358. **Tetracycline in the Treatment of Typhoid Fever**
F. RUIZ SÁNCHEZ, A. RUIZ SÁNCHEZ, and Q. F. ELBA NARANJO GRANDA. *Antibiotic Medicine* [*Antibiot. Med.*] **1**, 30–36, Jan., 1955. 9 refs.

Writing from the University of Guadalajara, Mexico, the authors describe the results in 25 cases of infection with *Salmonella typhosa* which they treated with tetracycline (" achromycin ") in a dosage of 50 to 100 mg. per kg. body weight per day given in three equal portions after meals in courses lasting up to 12 days. A comparison with the results obtained in another series, treated with chloramphenicol, was made on the basis of the time required for the patient to become afebrile. All the patients recovered, the rate of recovery being correlated with the severity of the illness and the stage at which treatment was begun; there was only one case of relapse.

Discussing the results the authors note that the time taken for the temperature to become normal varied widely. On the basis of temperature reduction alone they found tetracycline rather more useful than aureomycin (chlortetracycline), yet the over-all results obtained with it were inferior to those with chloramphenicol, which must therefore still be considered the drug of choice in the treatment of typhoid fever. *I. A. B. Cathie*

359. **Tetracycline in Typhoid Fever**
K. C. WATSON. *Lancet* [*Lancet*] **1**, 646–647, March 26, 1955. 12 refs.

Six patients with typhoid fever were treated with tetracycline. The response observed was poor, and for the treatment of this disease tetracycline seems to be considerably less useful than chloramphenicol.—[Author's summary.]

360. **The Combined Use of Cortisone and Chloramphenicol in the Treatment of Typhoid Fever.** (L'associazione cortisone–cloroamfenicolo nella terapia della febbre tifoide)
P. INTROZZI and S. MAINOLA. *Minerva medica* [*Minerva med. (Torino)*] **1**, 213–220, Jan. 27, 1955. 6 figs., bibliography.

From the University of Pavia the authors report the results of treatment with cortisone, alone and with chloramphenicol, of 42 patients (17 male, 25 female) ranging in age from 4 to 71 years, 39 of whom were suffering from typhoid fever and 3 from paratyphoid B. In 36 cases the diagnosis was confirmed both bacteriologically and serologically, while in the remaining 6 the bacteriological examination was negative but the results of the Widal reaction were regarded as positive.

The first 4 patients were treated with cortisone alone, injected intramuscularly. During the first 24 hours they received 300 mg. in 3 equal doses and on the second day 200 mg. in 2 equal doses, while in the more serious cases another 100 mg. was given on the third day. The temperature subsided, but 6 to 8 days after treatment was stopped a new increase of temperature occurred; this subsided after further treatment with cortisone and was followed by complete recovery. The other patients were treated with chloramphenicol (0·05 g. per kg. body weight daily for 5 to 6 days) in combination with cortisone in the above dosage. There was a rapid fall of temperature, sometimes within 8 hours of starting treatment. The majority were afebrile in 24 hours, and only in the most serious cases was defervescence delayed as long as 3 days. Enlargement of the spleen disappeared in 3 or 4 days and the rash subsided in 2 or 3 days. All patients tolerated both the hormone and the antibiotic well, and there were no side-effects. Apart from one patient who died from a chronic myocarditis, all recovered and were discharged 25 to 30 days after admission to hospital. *Franz Heimann*

361. **The Chemotherapy of Echinococcosis.** (La chimiothérapie de l'échinococcose)
JEAN THIODET, JACQUES THIODET, and C. BOULARD. *Thérapie* [*Thérapie*] **9**, 668–673, 1954. 2 refs.

The authors first review briefly the efforts that have been made in the last 50 or 60 years to find a safe and effective chemotherapeutic agent which, when given by intramuscular or intravenous injection, would cause regression and ultimate death of hydatid cysts. For a time the arsenobenzenes had a vogue, but early hopes were not confirmed. In the Argentine adult worms have been eradicated from animals by administration of arecoline hydrobromide in doses of 4 mg. per kg. body weight. Other South American workers have been investigating the possibility of the " biological " treatment of hydatid cyst with antigens. In 1951 Cuervo García in Spain showed that thymol was effective against hydatid cysts in sheep and rabbits, and treated 12 human patients with satisfactory results. One, who had a large hydatid in the liver, submitted to laparotomy after 3 months' treatment, when the cyst was found to have shrivelled and the disorganized, syrupy contents were non-infective to rabbits. On the basis of this report the present authors have used a preparation consisting of 1·5 g. of thymol made up to 3 ml. with olive oil containing 1% of iodine. An intramuscular injection is given on alternate days for one month, the course being repeated if necessary. Clinical details are given of 5 cases treated with this preparation [presumably somewhere in the Tropics] in all of which hydatid cysts (in the liver in 4 cases and in the lungs in one) regressed, with complete disappearance of symptoms in 3 cases and marked improvement in 2. The authors [rightly] recommend a more extensive trial of this method.
Clement Chesterman

Tuberculosis

362. Primary Tuberculosis in the First Year of Life. (La tuberculose initiale de la première année de la vie)
M. KAPLAN, P. STRAUS, and A. FISCHGRUND. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **30**, 4103–4110, Nov. 22, 1954. 11 figs.

The authors report a study carried out at the Hôpital Hérold, Paris, between 1951 and 1954 of 35 cases of primary tuberculosis occurring in infants under one year of age. More than half of these children were infected during the first 6 months of life, the source of infection being familial in 24 of the 28 cases in which it could be ascertained. In 5 cases there were no symptoms, while in 17 the symptoms were non-specific, consisting in loss of, or failure to gain, weight, cough, pyrexia, anorexia, and vomiting. In 7 cases the symptoms were those produced by pressure of an enlarged lymph node, such as a crowing type of cough, dyspnoea, or wheezing. Five of the 6 cases of tuberculous meningitis presented with neurological symptoms. There was one case of tuberculous bronchopneumonia, the remaining 28 being cases of simple primary infection.

There were 6 deaths in the series, 4 of these being of patients with meningitis. The radiographic appearances are described in detail. In most cases these appearances had returned to normal between the end of the fourth month and the first year. In 9 cases tubercle bacilli were found in the gastric contents, but there appeared to be no relation between the radiographic appearances and positive bacteriological findings. In 2 cases no chemotherapy was given, but all the remaining patients received PAS, streptomycin, or isoniazid for periods of between 2 and 12 months. In the authors' experience the principal advantage of chemotherapy in primary infections appears to be in preventing complications arising from dissemination of the bacilli; apart from this, however, chemotherapy does not appear to influence the course of the primary lesion. *T. M. Pollock*

363. Clinical Use of Potassium *para*-Aminosalicylate (KPAS)
L. MOLTHAN, R. V. COHEN, and C. J. D. ZARAFONETIS. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **71**, 220–227, Feb., 1955. 2 figs., 7 refs.

The potassium salt of *para*-aminobenzoic acid is known to be better tolerated than its sodium salt; as this acid is closely related to *p*-aminosalicylic acid (PAS) the authors carried out a trial with the potassium salt of PAS (KPAS) in order to determine the incidence of side-reactions to the drug and also its "patient-acceptance".

At various Pennsylvanian hospitals a total of 64 patients (60 with pulmonary tuberculosis, 2 with tuberculous disease of the hip, one with Pott's disease, and one with tuberculous cervical adenitis) were treated with KPAS for 9 months. Patients with histories of intolerance to PAS were deliberately included in the trial. The drug was given by mouth as a 10% solution in tap water, at first in smaller doses but after 2 weeks in a dosage of 12 g. per day divided in 4 doses.

It was found that KPAS was well tolerated and that the side-effects associated with PAS medication (anorexia, nausea, vomiting, and diarrhoea) were not common to the potassium salt. Of 38 of the patients who had previously been intolerant of either PAS or sodium PAS, only 3 could not take 12 g. of KPAS daily, because of the development of haemorrhoidal bleeding, anorexia, and personality changes respectively. The remaining patients, who had not had previous PAS treatment, all tolerated KPAS perfectly. Non-tuberculous complications were present in 18 patients, including 9 cases of renal insufficiency; these patients took the drug well and no adverse effects were noted, even among those with gastrointestinal disease. The performance of routine blood counts, urine analysis, blood urea nitrogen and serum potassium determinations, and conventional liver function tests revealed no evidence of toxicity. The plasma PAS concentration was determined on samples of plasma from 26 patients taking KPAS and compared with those from 15 receiving the parent acid; this showed that KPAS produced an adequate blood concentration of PAS and that it was more rapidly and more completely absorbed than PAS.

The authors point out that exposure to light alters the solution of KPAS, and it is recommended that it should be freshly made up each day or kept in a refrigerator. If these precautions are taken KPAS offers a superior means of PAS therapy, is without toxic effects, and is well tolerated by the patient.

Thomas Marmion

DIAGNOSIS AND PROPHYLAXIS

364. The Middlebrook–Dubos Hemagglutination Test for Tuberculosis in Children and Adults
A. JOSIUKAS, T. E. ROY, and G. BOYD. *Journal of Clinical Investigation* [*J. clin. Invest.*] **33**, 1415–1422, Nov., 1954. 4 figs., 43 refs.

Further evidence is here presented from the University of Toronto to show that the Middlebrook–Dubos haemagglutination test, as currently performed, is of little value in the diagnosis or prognosis of tuberculosis. Of interest, however, is the finding that positive reactions could be evoked in experimental animals by the injection of such apparently unrelated materials as diphtheria toxoid, a mixed vaccine of nasopharyngeal organisms, and a saprophytic mycobacterium. The authors consider that the increase in the incidence of false positive reactions with age in human subjects might be due to exposure to such antigens in the past, and that until

antigens specific to pathogenic strains of *Mycobacterium tuberculosis* are found which are capable of sensitizing erythrocytes the test is unlikely to be useful clinically.

J. E. M. Whitehead

365. **Tuberculin Test Comparison between the Heaf Multiple Puncture Apparatus and the Mantoux Test**
C. L. GREENING. *Central African Journal of Medicine* [*Cent. Afr. J. Med.*] **1**, 25–29, Jan., 1955. 4 refs.

As a preliminary to a B.C.G. vaccination campaign in Northern Rhodesia the author carried out a comparative study of the Mantoux test and the Heaf multiple-puncture test using purified protein derivative (P.P.D.). Of a total of 1,418 African subjects tested, 1,164 reported back for examination after 72 hours. The tests with the Heaf multiple-puncture apparatus—which was modified and considerably improved in the course of the experiment—picked out all Mantoux-positive individuals at a level of 10 units, the critical diameter of the reaction being fixed at not less than 5 mm. The test was found to be more rapid, more reliable, and less painful (an important consideration in dealing with young children) than the Mantoux test and is therefore being employed alone for the detection of tuberculin allergy in the campaign.

The author draws attention to an acuminate, non-specific type of reaction which accompanied the normal Heaf reaction in some cases and which does not seem to have been described previously. In a number of cases also, owing to the unusually thin skin of the subject, the P.P.D. was administered by the Heaf apparatus subcutaneously instead of intradermally, giving rise to difficulty in reading the reaction and, in a few instances, to a false negative reading; it is therefore recommended that all Heaf-negative vaccination sites should be palpated as well as inspected visually. *R. Crawford*

366. **B.C.G. Vaccination**
F. R. G. HEAF. *Lancet* [*Lancet*] **1**, 315–320, Feb. 12, 1955. 31 refs.

RESPIRATORY TUBERCULOSIS

367. **The Diagnostic and Prognostic Significance of the Eosinophil Count in Tuberculosis of the Lungs in Children.** (О диагностическом и прогностическом значении содержания эозинофилов в периферической крови при туберкулезных инфильтрациях легких у детей)
A. L. KNIREL. *Педиатрия* [*Pediatrija*] 66–77, No. 1, Jan.–Feb., 1955. 1 fig.

Tuberculous infiltration of the lungs is rare in children and difficult to diagnose, but when a correct diagnosis leads to early treatment, serious complications can usually be avoided and the prognosis is good. At the Stalin Medical Institute, Krȳmsk, 231 children with infiltrative lesions were studied between 1944 and 1948. They fell into three groups: (1) 142 had an acute flare-up of an infiltrative pulmonary focus; (2) 37 had chronic pulmonary infiltration; and (3) 52 had a progressive type of disease, such as caseous pneumonia or miliary tuberculosis, with or without clinical manifestations of extra-pulmonary tuberculosis in the skeletal, lymphatic, or alimentary system. The eosinophil count in the peripheral blood was determined in each case and the three groups further subdivided accordingly, as follows:

Eosinophil Count	Group 1	Group 2	Group 3
Normal (1·5 to 3%) ..	45·6%	54·2%	40·4%
Eosinopenia (0 to 1%)	39·4%	29·7%	55·8%
Eosinophilia (3 to 10%)	15%	16·1%	3·8%

From these findings it is concluded that a tendency towards eosinopenia indicates progression of the tuberculous process and that a normal or increased count is associated with a favourable prognosis and quiescence of the disease. *Edward D. Fox*

368. **A "Follow-up" Chest *X*-ray Survey in the Rhondda Fach. I. Pulmonary Tuberculosis**
A. L. COCHRANE, J. G. COX, and T. F. JARMAN. *British Medical Journal* [*Brit. med. J.*] **1**, 371–378, Feb. 12, 1955. 12 figs., 10 refs.

One of the objects of the field experiment undertaken by the Pneumoconiosis Research Unit of the Medical Research Council in the Rhondda Fach was to examine the effect on the morbidity and mortality from tuberculosis of the removal from a community of all known infectious cases of the disease at a given point of time. The first stage in this experiment was carried out in 1950–1, when an *x*-ray survey of some 90% of the inhabitants of the Rhondda Fach over 5 (23,600) was made, 112 infectious cases were discovered, and the prevalence of infectious, active, and quiescent cases was ascertained (Cochrane *et al.*, *Brit. med. J.*, 1952, **2**, 843; *Abstracts of World Medicine*, 1953, **13**, 282). It was of course impossible entirely to prevent all the patients who were considered to be suffering from active tuberculosis from circulating amongst the general population of the area, yet all but 2 accepted hospital treatment for a period, and after discharge were kept under strict supervision. By 1953, 14 had died, 3 had removed from the district, and 35 were still sputum-positive—"a rude reminder," say the authors, "that the therapeutic battle is only half won".

The results of thus controlling the infector pool form the subject of the present report. In 1953, after a lapse of 2½ years, a similar proportion of the population of the area was again radiographed. Among females some decline in the prevalence of tuberculosis, varying in degree with age, was apparent—for example, in the age group 20 to 24 the incidence of active tuberculosis (including infectious cases) was reduced from 37 to 17 per 1,000, whereas the over-all rate for females of all ages fell from 10·3 to 6·9 per 1,000, the incidence of infectious cases being reduced from 6·0 per 1,000 to 3·1 per 1,000. A similar fall in prevalence of the disease had occurred among miners of the younger age groups and ex-miners, but the rate among older miners showed a slight increase.

(The rates for non-miners are difficult to interpret owing to their atypical age distribution.) Except among miners, mortality from tuberculosis in the years between the surveys fell to a greater extent in the Rhondda Fach than in the rest of the urban area of which it forms a part [but the number of deaths on which these rates were based must have been very small].

Of the 21,068 persons radiographed in 1950–1, 2·5% (523) had died and 7% (1,495) had removed from the area; of the remaining 19,050, 18,127 (95·2%) were re-examined in 1953. Among those whose radiograph was regarded as normal in 1951, 46 new cases of tuberculosis were found to have developed—almost all in persons between the ages of 15 and 34. The annual radiological attack rates per 1,000 are given as follows:

	Females	Males (without pneumoconiosis)
Age 15 to 24	2·8	4·7
Age 25 to 34	0·7	1·0

[These attack rates do not contribute materially to the solution of the specific problem, since they cannot be compared with similar rates for the Rhondda Fach for any period preceding the experiment, nor with rates from other areas at the same point of time. But they stress once more what has been pointed out so often in recent literature, that whereas the peak of mortality from tuberculosis among females occurs in the age group 25 to 34 and among males in the age group 65 to 74, the attack rate is highest amongst young adults of both sexes.]

The authors discuss the imperfections of attack rates and mortality rates as indices of the prevalence of tuberculosis, and suggest that prevalence rates based on *x*-ray surveys in other areas would be very valuable.

E. Lewis-Faning

369. **The Behaviour of Pulmonary Tuberculous Lesions. A Pathological Study**
E. M. MEDLAR. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **71**, 1–244, March, 1955. 136 figs., 46 refs.

370. **The Gastric Mucosa in Pulmonary Tuberculosis.** (La muqueuse gastrique des tuberculeux pulmonaires)
J. VAGUE, H. BONNEAU, and M. LEGRÉ. *Presse médicale* [*Presse méd.*] **63**, 112–113, Jan. 29, 1955.

The authors have studied the gastric mucosa in 128 cases (100 men and 28 women, aged 22 to 77) of chronic tuberculosis by means of aspiration biopsy of the mucous membrane (103 cases), and by test meals following subcutaneous injection of histamine. In all cases also a complete clinical and radiological examination of the digestive tract was carried out, and gastroscopy was performed in 15 cases.

Of the 103 cases examined by biopsy, 51 showed an abnormal gastric mucosa, which was of two types: (1) simple inflammatory gastritis, and (2) inflammatory gastritis with an atrophic mucous membrane. Of the whole series of patients, 24% suffered from dyspepsia, 7% from heartburn, and 14% from diarrhoea. A rough correlation was found between these symptoms and the presence of hypochlorhydria or achlorhydria, although the authors point out that these conditions may be hereditary and that their incidence normally increases with age. In the present series 77% of the cases showed either an achlorhydria or hypochlorhydria after histamine injection.

The authors discuss the aetiology of the mucosal lesions, which are more frequent in patients with chronic tuberculosis and producing large amounts of sputum. One complicating factor in this study was the high proportion of alcoholic subjects; among these there was a tendency to epithelial lesions of the gastric mucosa. In spite of this the authors feel that the chief factor in the production of gastritis in these patients is the swallowing of infected sputum.

G. M. Little

371. **A Clinical Appraisal of Cyanacetic Acid Hydrazide in Chronic Pulmonary Tuberculosis**
T. MARMION. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **49**, 9–19, Jan., 1955. 15 refs.

Since March, 1954, at the Sanatorium Angleterre, Davos, Switzerland, 31 patients with chronic pulmonary tuberculosis have been treated with cyanacetic acid hydrazide (C.A.H.). All except 2 of these patients had already received "large quantities" of other antituberculous drugs, and of 10 who were known to be sputum-positive, 6 had developed resistance to these drugs. Over half of the patients had been subjected to various surgical procedures.

A maintenance dose of 8 mg. of C.A.H. per kg. body weight was given daily for periods up to 5 months. Although there was no important change in physical signs or symptoms, radiological improvement was noted in 15 cases, this being marked in 5. The erythrocyte sedimentation rate fell to within normal limits in all except one. In 4 cases the drug had to be discontinued because of severe side-effects, which included conjunctivitis, urticaria, headache, and paraesthesiae. The author believes that C.A.H. will prove to be a useful drug for patients unable to tolerate isoniazid, and of considerable value in the treatment of chronic tuberculosis.

E. G. Rees

372. **Central Nervous System Complications during I.N.H. Treatment of Pulmonary Tuberculosis**
M. M. WOOD. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **49**, 20–29, Jan., 1955. 6 figs., 8 refs.

Manifestations of nicotinic acid deficiency in patients treated with isoniazid may be the result of the antimetabolic action of the latter drug. The author, from King George V Hospital, Durban, describes his findings in 20 Bantu patients with pulmonary tuberculosis who were given isoniazid. In 4 patients a confusional psychosis developed during treatment; one of these patients had no further mental symptoms after isoniazid was withdrawn, but 3 required nicotinic acid therapy. In 13

patients who were pellagrous on admission it was found that the lesions of pellagra could not be treated satisfactorily on a good diet, even with vitamin supplements, if isoniazid was given concurrently. The author suggests that once a patient is "saturated" with nicotinic acid isoniazid therapy may be instituted with safety; he recommends a daily maintenance dose of 50 mg. of nicotinic acid when the daily therapeutic dose of isoniazid is 400 mg. *E. G. Rees*

373. **Experience with Pyrazinamide**

B. P. POTTER and S. F. CHANG. *Diseases of the Chest* [*Dis. Chest*] **27**, 44–50, Jan., 1955. 7 refs.

The authors report, from Nassau County Sanatorium, New York, the results in 60 cases of pulmonary tuberculosis treated with pyrazinamide, a nicotinic acid derivative related to isoniazid. In 27 cases treatment was with pyrazinamide alone, and in the remainder with pyrazinamide in combination with streptomycin or PAS. Patients were selected who had had ample treatment by bed rest, and all but 4 of them had previously received one or more courses of streptomycin and PAS but had failed to respond. Pyrazinamide was given in a dosage of 3 g. daily divided into 4 equal doses; in combined treatment 1 g. of streptomycin was given twice weekly or 8 to 12 g. of PAS daily in addition.

Regressive radiological changes were observed in 13 cases (21·6%). Of these 13, cavitation was present in 3 but in not a single instance was cavity closure effected. Toxic effects were disturbing, in that a high incidence of hepatitis and severe haemoptyses was encountered, there being 8 cases of the former with one death, and 8 of the latter with 7 deaths. In view of this marked toxicity the view is expressed that the use of pyrazinamide should be discouraged, particularly as there was also some evidence that resistant strains of tubercle bacilli emerge early during treatment with pyrazinamide. *John Taubman*

374. **Experiences in the Management of Long-standing Chronic Cases of Pulmonary Tuberculosis Treated with Isoniazid for One Year**

H. T. OVERBY and R. W. WOLIUNG. *Diseases of the Chest* [*Dis. Chest*] **27**, 51–58, Jan., 1955. 2 figs.

Writing from Dunham Hospital, Cincinnati, Ohio, the authors describe the management of 38 patients suffering from far advanced, chronic, bilateral pulmonary tuberculosis. The patients were chosen at random from a large number of patients regarded as "good chronic" cases. The median age was 53 years (range 19 to 76) and 24 of the patients had previously had courses of streptomycin with PAS. The average period of hospitalization at the beginning of this study had been 37 months.

Isoniazid in a dose of 250 mg. daily was given alone for one year. Marked improvement in the amount of cough and sputum was noted and all patients showed gains in appetite and weight associated with a sense of well-being. Radiological improvement, however, lagged behind clinical improvement; for example, at the end of 3 months 10 showed demonstrable improvement, but in most cases this was very slight. At the end of 9 months 3 patients were sufficiently improved radiologically and clinically to be discharged from hospital, and at the end of one year 3 more were discharged, the disease being considered to be arrested. Only 2 cases showed progression of the disease radiologically. In 7 cases the sputum converted to negative and remained so for the entire year. At any given time during the study the incidence of positive sputa was less than 50%, whereas before the institution of isoniazid therapy over 94% of sputa were positive.

In 2 cases in which the sputum remained positive culture studies and guinea-pig inoculation at the end of 8 months of treatment were negative. In these 2 cases, it is suggested, the bacillus may have been altered by isoniazid to such an extent that it was no longer pathogenic. *John Taubman*

375. **Various Combinations of Isoniazid with Streptomycin or with P.A.S. in the Treatment of Pulmonary Tuberculosis**

MEDICAL RESEARCH COUNCIL TUBERCULOSIS CHEMOTHERAPY TRIALS COMMITTEE. *British Medical Journal* [*Brit. med. J.*] **1**, 435–445, Feb. 19, 1955. 18 refs.

The present report is the seventh made to the Medical Research Council by their Tuberculosis Chemotherapy Trials Committee, and describes the response of a total of 588 patients with pulmonary tuberculosis at 51 hospitals in Great Britain to the following four treatment schedules. All the patients received 200 mg. of isoniazid daily in two equal doses by mouth, and in addition: (1) 182 patients were treated with 1 g. of streptomycin daily (Group SH); (2) 142 with 1 g. of streptomycin twice weekly (Group S2H); (3) 159 with 20 g. of sodium PAS daily in 4 equal doses by mouth (Group 20PH); and (4) 105 with 10 g. of sodium PAS daily in 2 equal doses by mouth (Group 10PH). Each treatment was given for the first half of a 6-month period of observation. During the 3-month period of treatment, 7 deaths occurred, 2 among patients in Group SH, 3 in Group 20PH, and 2 in Group 10PH. No severe toxic reactions to isoniazid were noted, but treatment had to be abandoned in 7 cases because of a severe toxic reaction, attributed in 6 of these to PAS and in the remaining case to streptomycin.

At the end of the period of treatment radiological improvement was noted in 84% of patients in Group SH, 75% in Group S2H, 76% in Group 20PH, and 76% in Group 10PH. Cases showing the most marked improvement occurred most frequently in Group SH. A gain in weight of 14 lb. (6·4 kg.) or more occurred in 38, 58, 41, and 48% respectively of the patients in the four treatment groups, the average over-all gains for the groups being 11·3 lb. (5 kg.), 14·8 lb. (6·7 kg.), 11·3 lb., and 13·9 lb. (6·3 kg.) respectively. The response in respect of improvement in the general condition, reduction of temperature, and lowering of the erythrocyte sedimentation rate at 3 months was roughly similar in the four groups. Bacteriologically, after one month of treatment the proportions of patients with sputum shown to be negative by smear and culture were 40, 33, 34, and

34% respectively. At the end of 2 months these proportions had increased to 55, 53, 49, and 53% respectively, and after 3 months a further increase occurred to 75, 74, 73, and 75% respectively.

At the end of 3 months two strains resistant to isoniazid were obtained from 22 patients with positive cultures in Group SH, 12 from 30 patients with positive cultures in Group S2H, none from 24 such patients in Group 20PH, and 2 from 25 such patients in Group 10PH. Thus, whereas few patients in Groups SH, 20PH and 10PH developed resistant strains, a high proportion (40%) of those in Group S2H did so. At the same period no strains resistant to streptomycin were isolated from 22 positive cultures in Group SH, compared with 3 streptomycin-resistant strains from 31 positive cultures in Group S2H. Only one strain resistant to PAS was isolated from 22 positive cultures in Group 20PH, and one from 23 positive cultures in Group 10PH.

In a small number of cases the treatment described was continued after the 3-month period, although in some the dosage was changed. Sensitivity tests carried out at 4, 5, and 6 months respectively showed results which differed little from those obtained at 3 months, although there was a greater tendency to the emergence of resistance to isoniazid in Group S2H than in the other groups.

[For further details of the results of this study, which are presented in numerous tables, the original paper should be consulted.] *G. M. Little*

376. **Chemotherapy in a Cairo Chest Clinic. A Preliminary Report on the Methods Adopted in Assessing the Value of Isoniazid, Streptomycin and Paraminosalicylic Acid in 122 Cases of Pulmonary Tuberculosis**
A. IBRAHIM, A. BOUTROS, and J. B. MCDOUGALL. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **49**, 38–49, Jan., 1955. 6 figs., 6 refs.

377. **A Five-year Follow-up Study of Sixty-four Tuberculous Patients Treated with Streptomycin in 1947–1948**
J. MONROE, N. S. LINCOLN, R. HORTON, and F. L. ARMSTRONG. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **71**, 193–200, Feb., 1955. 6 refs.

At four tuberculosis hospitals in New York State 64 patients with pulmonary tuberculosis were treated with streptomycin in 1947–8, and the late results of this treatment were assessed in June, 1954. The series included patients of all age groups and embraced all stages of the disease and the more common extrapulmonary complications. In 13 cases streptomycin was given in dosages ranging from 1 g. twice a day to 1 g. every other day for periods of up to 6 months. In the remaining 51 cases three treatment schedules were used, one-third of the patients receiving 1 g. daily for 2 months, one-third 1 g. daily for 3 months, and one-third 1 g. twice daily for 3 months.

During the period of treatment the disease regressed in 53 cases, showed no change in 8, and became worse in 3. Of the 11 patients showing no improvement, 6 died during the follow-up period, and all of these belonged to the short-term (2 months) treatment group. A further 6 deaths occurred amongst those who had been treated for longer periods. Of the 12 patients who died, 10 had tuberculous complications, which had either been present at the start of the observation period or had appeared during the subsequent 5 years. In all, 13 patients developed complications after the initial course of streptomycin. Additional drug therapy was necessary in 26 cases during the follow-up years, and a further 33 patients underwent surgical procedures. Most of the patients who required re-treatment did so in the first half of the follow-up period, and it was in these 2½ years also that the majority of the deaths occurred. It was recognized at an early date that streptomycin treatment was not definitive.

The conclusions arrived at from this study are as follows: (1) over three-quarters of the patients treated with streptomycin in 1947–8 were alive in 1954 (although admittedly other forms of treatment were given to approximately half of them later in the period); (2) streptomycin and subsequent treatment did not prevent the development of tuberculous complications; (3) the original courses of streptomycin were too short; and (4) in determining the long-term prognosis in such cases the duration of streptomycin therapy is a factor of great import. *Thomas Marmion*

378. **Viomycin in the Treatment of Pulmonary Tuberculosis.** (La viomicina en el tratamiento de la tuberculosis pulmonar)
J. ZAPATERO, F. GARCÍA-MORENO, J. CALDERÓN MONTERO, J. MONTURIOL, and M. GARCÍA VALENCIANO. *Revista española de tuberculosis* [*Rev. esp. Tuberc.*] **24**, 1–28, Jan., 1955. 25 refs.

After a review of the literature concerning the isolation and properties of "viomycin" (viocin), the authors describe their experience of the clinical use of this drug and compare it with that of other investigators. Viocin was used at the General Hospital, Madrid, in the treatment of 12 cases of pulmonary tuberculosis, all but one having a positive sputum, and cavitation being present in all but 2. Nearly all the patients had had previous chemotherapy. The dosage was 2 g. twice weekly for 2 months, PAS being given at the same time in daily doses averaging 10 g. Radiologically, there was some improvement in the 2 cases without cavitation, but in only 3 of the remaining 10 was there any reduction in cavity size. Bronchial lesions in 2 cases were unchanged. There was some subjective improvement, but even this was mostly confined to the first month and was considerably inferior to that following isoniazid. In 2 cases the sputum became negative for tubercle bacilli and in 8 cases there was a reduction in the number of bacilli in the sputum. In all cases there was a reduced sensitivity to tuberculin at the end of treatment. No toxic manifestations were noted.

The authors were obviously not very impressed with the results of treatment with viocin, but they suggest that the drug may be useful in patients who have become resistant to the standard antibiotics. *Paul B. Woolley*

EXTRA-RESPIRATORY TUBERCULOSIS

379. **Tuberculous Disease of the Parotid**
D. H. PATEY and A. C. THACKRAY. *Archives of the Middlesex Hospital* [*Arch. Middx Hosp.*] **4**, 256–262, Oct., 1954. 6 figs., 5 refs.

Tuberculosis of the parotid gland in the absence of tuberculous disease elsewhere in the body is probably less rare than has been supposed. In this paper from the Middlesex Hospital, London, the authors describe 6 cases of this condition. In 5 of these a lump was present in the parotid and was diagnosed as a mixed parotid tumour. In the 6th case the swelling was cystic and aspiration revealed caseous material. It is noteworthy that in 5 of the cases the swelling was in the facial portion of the parotid gland.

A point made by the authors [which is perhaps not generally recognized] is that normal parotid lymph nodes differ from those found elsewhere in being composite structures, " the features of a lymph node being grafted on to a parotid lobule ". Intraparotid lymph nodes may contain epithelial ducts of parotid type, and a similar finding has been shown in nodes outside the anatomical limits of the gland. Thus a tuberculous parotid nodule may be inside or outside the parotid capsule, and if outside may well be mistaken for a high cervical tuberculous lymph node.

Discussing aetiology, the authors suggest that the predilection for the facial part of the parotid gland raises the possibility that the infection comes from the mouth along the parotid duct. *K. Whittle Martin*

380. **Streptokinase–Streptodornase in the Local Treatment of Suppurative Extrapulmonary Tuberculosis**
G. N. HAZLEHURST. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **71**, 1–11, Jan., 1955. 6 refs.

This report from the New York University College of Medicine and Bellevue Hospital, New York, details the treatment of 11 patients with suppurative tuberculous lymphadenitis (17 lesions), 2 with cold abscesses, and one with tuberculous tenosynovitis in which streptokinase–streptodornase (" varidase ") was used. The varidase was administered at first by irrigation of the incised fluctuant area with 30 to 60 ml. of saline containing 1 or 2 ampoules of the preparation (each ampoule containing from 150,000 to 300,000 units of streptokinase and from 75,000 to 250,000 units of streptodornase). Later it was incorporated in a jelly made by mixing gum tragacanth and sodium alginate in isotonic Sorensen's buffer and adjusting to *p*H 7·5. The lesions were treated daily. Antituberculous drugs were given concomitantly in some cases.

Most of the cases of lymphadenitis, which ranged in duration from one week to 6 months, were in children. In all but one the diagnosis was confirmed bacteriologically. The period of treatment varied from a few days to 7 weeks (commonly 7 to 10 days) and healing occurred in all cases, usually within 3 weeks. Most of these cases have been followed up for many months, but no recurrences and no toxic effects have so far been noted.

The 3 patients with other types of lesion needed longer treatment, but healing occurred ultimately in 2 cases. The third, a case of long-standing Pott's disease with psoas abscess in a man of 68, was complicated by infection with *Proteus vulgaris*, and although healing of the sinuses occurred eventually, the subsequent course of the disease is unknown. The action of these enzymes is discussed, and although the author admits that the rationale of their use is not fully understood, he claims that it is amply justified by the results.

R. J. Matthews

381. **Studies on the Intrathecal Use of Streptokinase–Streptodornase in Tuberculous and Other Types of Bacterial Meningitis**
G. N. HAZLEHURST. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **71**, 12–29, Jan., 1955. 1 fig., 20 refs.

The intrathecal injection of streptokinase–streptodornase in the form of " varidase " was used as an adjunct to antibacterial therapy in the treatment of 6 patients (3 under 7 years old and 3 over 11) with tuberculous meningitis and 4 patients (2 infants and 2 middle-aged) with acute purulent meningitis at Bellevue Hospital (New York University College of Medicine). To determine the toxicity of the preparation, 6 subjects with normal cerebrospinal fluid (C.S.F.) were first given small doses of varidase (20 units of streptokinase and 4 units of streptodornase in the first case, and 200 units and 40 units respectively in the other 5), and the C.S.F. was subsequently examined for enzyme content and lytic activity. The dosage of varidase in the cases of meningitis ranged from 5,000 to 30,000 units of streptokinase and 1,000 to 7,500 units of streptodornase.

The clinical features and treatment of each case are described in considerable detail [for which reference must be made to the original text]. In general, it appeared that the severity of the reaction to the intrathecal injections of these enzymes was in inverse proportion to the degree of meningeal damage present. Thus the toxic effects were much more severe in the normal subjects and in the older patients with tuberculous meningitis than in patients who were more acutely ill. It was found also that when the toxic reaction was severe no active enzyme systems could be demonstrated in the C.S.F., whereas when there was no reaction such systems could be demonstrated for several hours after the injection of varidase. The end-results in the cases of acute meningitis were encouraging, all 4 patients ultimately recovering. By contrast 5 out of the 6 patients with tuberculous meningitis died—usually from a relapse—within a few months, although in several there was improvement initially; the fate of the sixth patient is unknown. It should be pointed out, however, that in all the cases treated the prognosis was originally regarded as poor.

[Both this paper and the one immediately preceding it (Abstract 380) merit particular attention on account of the detailed information given.] *R. J. Matthews*

Venereal Diseases

382. **Avoidable Congenital Syphilis.** (Über vermeidbare connatale Lues)
J. Brock and E. H. Grüner. *Ärztliche Wochenschrift* [*Ärztl. Wschr.*] **10**, 185–188, Feb. 25, 1955. 4 refs.

The incidence of prenatal and congenital syphilis is declining in Germany as in many other countries, and the authors are of the opinion that it might be possible, by means of a programme of prenatal prophylaxis, to eradicate congenital syphilis completely. For this purpose they recommend that in addition to the routine blood testing of pregnant women, examination of the retroplacental blood should be carried out, false positive reactions being excluded with the treponemal immobilization test. All pregnant women who have previously been treated for syphilis should receive two courses of penicillin during pregnancy, since their syphilis may become reactivated, while babies born of untreated syphilitic mothers should receive immediate preventive treatment with penicillin, even in the absence of clinical or serological evidence of infection. (It is pointed out that in Germany, under a law passed in 1953, a pregnant woman must undergo such treatment as may be considered necessary to safeguard the baby against infection, while it is the duty of the parents to ensure that the baby receives any treatment recommended by the physician.)

The case histories of 4 babies admitted during the period 1949–51 to the Rothenburg District Children's Hospital, Hamburg, with congenital syphilis are quoted. In each case the child was apparently normal at birth but developed signs of syphilis and a positive serum reaction 3 to 10 weeks later.

[There are serious objections to the replacement of clinical and serological observation of apparently healthy babies born of syphilitic mothers by " preventive treatment ". Amongst other drawbacks is the possibility that a child treated in this way may be stigmatized for life as having had congenital syphilis. The case histories are not at all convincing as evidence of the need for such a policy, because neither the mothers nor the babies had had adequate serological surveillance. For example, only one of the mothers had had her blood tested during pregnancy, and in 3 cases the baby's blood was not tested until syphilis became clinically apparent.]

A. Fessler

383. **Untreated Syphilis in the Male Negro. Pathologic Findings in Syphilitic and Non-syphilitic Patients**
J. J. Peters, J. H. Peers, S. Olansky, J. C. Cutler, and G. A. Gleeson. *Journal of Chronic Diseases* [*J. chron. Dis.*] **1**, 127–148, Feb., 1955. 11 refs.

This is a further report of the results of the " Tuskegee Study " of untreated syphilis in the male negro which has been in progress since 1932 under the Venereal Disease Program of the U.S. Public Health Service at Tuskegee, Alabama. The post-mortem findings in a controlled group of untreated syphilitic and non-syphilitic subjects are here correlated with the serological and clinical findings. Between 1933 and 1952, 165 (40%) of the 408 untreated syphilitics and 51 (27%) of the 192 comparable control subjects studied have died, necropsy being carried out on 92 (56%) of the former and 33 (65%) of the latter. The age distribution in these last two groups was similar, approximately half of each being under and half over 65 at death.

Lesions characteristic of syphilitic involvement of the cardiovascular system were found in 89 of the 92 syphilitic subjects. Gross examination revealed syphilitic aortitis in 36 cases (40%), the most reliable and most highly pathognomonic signs being linear striation of the intima (32·6%) and saccular aneurysm (7·9%). Microscopically, only marked thickening of the aortic wall and necrosis of the media appeared to be pathognomonic of syphilis. Syphilitic aortitis was diagnosed microscopically in 41 (46%) of the syphilitic subjects, while in 4 (12·5%) of the control subjects minimal damage, conceivably due to syphilis, was present. Cardiac hypertrophy (heart weight over 400 g.) was present in 69·5% of the syphilitic group and 69·2% of the control group, and with the exception of syphilitic valvulitis (which was present in less than 10% of the former) no abnormality of sufficient specificity was found to justify a diagnosis of cardiac hypertrophy due to syphilis. Of the 89 syphilitics with cardiovascular lesions, the Kahn test was positive at the time of death in 60. Aortitis was diagnosed in 37 (62%) of these cases, but in 14 of them the diagnosis was based on either gross or microscopic findings alone and might be considered doubtful. The minimum incidence of aortitis in this group was therefore 38%. Among the syphilitics in whom the Kahn reaction was negative or doubtful at death, aortitis was diagnosed by both gross and microscopical examination in only 2 cases.

From these findings the authors estimate that in the male negro with untreated syphilis of more than 10 years' duration and who is seropositive at death, the likelihood of syphilitic cardiovascular involvement being demonstrable at necropsy is approximately 50%. Among the 62 cases in which the gross and microscopical findings in the aorta were in agreement there were only 2 cases in which syphilitic involvement was present but had not been diagnosed clinically, whereas in 19 cases a clinical diagnosis of syphilitic aortitis was not confirmed post mortem. No definite light was thrown by this study on the relation between syphilis and arteriosclerosis.

The central nervous system was examined post mortem in 46 of the syphilitic group and definite evidence of syphilis was found in only 2 cases, both in association with syphilitic aortitis. The authors remark that " the great scarcity of frank syphilitic involvement of the central nervous system and the complete absence of lesser lesions attributable to syphilis are noteworthy ".

No significant differences between the syphilitic and control groups were found in respect of lesions in the other systems of the body, which, it would seem, are not

commonly affected by syphilis. The primary cause of death in 18 of the 92 syphilitics on whom necropsy was performed was syphilitic involvement of the cardiovascular or central nervous systems; otherwise the distribution of causes of death in both groups was similar.

[The Tuskegee Study is unique, and further reports may be expected throughout the further period of 20 years which, it is anticipated, will be required for its completion.] *Leslie Watt*

384. **A Simple Procedure for the Identification of Non-syphilitic Reactions in Serologic Tests for Syphilis in Leprosy Patients**

J. PORTNOY and W. F. EDMUNDSON. *International Journal of Leprosy* [*Int. J. Leprosy*] **22**, 181–194, April–June, 1954. 31 refs.

Studies at the Venereal Disease Research Laboratory of the U.S. Public Health Service have shown that the addition of choline chloride to the antigen used in the V.D.R.L. slide test for syphilis raises its reactivity with syphilitic sera while reducing its reactivity with sera giving non-specific reactions. A differential test is described in which V.D.R.L. antigen is prepared and divided into equal portions; these are centrifuged at 2,500 r.p.m. for 15 minutes, the turbid supernatants discarded, and the walls of the tubes wiped dry. To one tube normal saline is added (Antigen I) and to the other 10% choline chloride (Antigen II), each in an amount equal to the volume of antigen originally centrifuged. Using these two antigens, slide flocculation tests are made as in the original V.D.R.L. technique, the results being read microscopically at a magnification of ×100 and the degree of flocculation with each antigen being assessed on a numerical scale reading from 0 (no clumping or very small clumps) to 4 (large clumps). Where necessary, quantitative tests on serial twofold dilutions of serum in saline starting at 1 in 2 are made and the result for each antigen expressed as the sum of the flocculation values obtained at the various dilutions. Where flocculation occurs only with Antigen I, or where the difference between the results with the two antigens is 3 or more, the reaction is regarded as non-syphilitic; where the difference is 2 or less the reaction is regarded as syphilitic; and where flocculation occurs with neither the serum is regarded as non-reactive.

There was good agreement between the results of this differential procedure and those of the treponemal immobilization (T.P.I.) test on sera from 84 presumed non-syphilitic patients, 87 with early syphilis, and 54 with late or late latent syphilis. Sera from 255 lepers were also studied; 14 of these were from patients with clinical or historical evidence of syphilis, 6 of which gave the syphilitic reaction in the differential test and positive or doubtful reaction in the T.P.I. test, 5 were non-reactive in the differential test and negative or doubtful or doubtful reactions in the T.P.I. test, 5 were non-syphilitic reaction in the differential test, two being T.P.I.-positive and one T.P.I.-negative. Of the 241 sera from lepers with no evidence of syphilis, 21 were found to be T.P.I.-positive; 15 of these gave syphilitic and 3 non-syphilitic reactions, and 3 were non-reactive with the differential test. Of the remaining 220 sera, which were all T.P.I.-negative, 153 were non-reactive and 67 gave the non-syphilitic type of reaction.

Substitution of sodium chloride for choline chloride in equimolar quantities gave an essentially similar degree of inhibition of the reactivity of sera giving non-specific reactions, but the " coarseness " of the negative reaction made the interpretation of results difficult.

A. E. Wilkinson

385. **The Value of the Quantitative Complement-fixation Test for Syphilis in Leprosy**

J. O. DE ALMEIDA, L. SOUZA LIMA, and R. P. S. CARVALHO. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **4**, 41–46, Jan., 1955. 17 refs.

At the University Faculty of Medicine, São Paulo, Brazil, complement-fixation tests for syphilis, employing a quantitative technique with cardiolipin and antigens from an extract of tubercle bacilli, were performed on samples of serum from 467 patients with treated and untreated lepromatous leprosy after the patients had undergone clinical examination in order to exclude tuberculosis. With the cardiolipin test there was a reaction in 28 cases (6%) and no reaction in the remainder. With the antigens from tubercle bacilli there was a reaction in 413 cases (88·4%) and no reaction in 54 (11·6%). Blood samples from 133 of the 439 leprous patients who gave negative results in the cardiolipin test were also tested by other techniques for the serodiagnosis of syphilis. Of these, 65% gave positive reactions with the Kahn standard test, 36% with the V.D.R.L. test, and 12·5% with the Kolmer antigen test.

The patients who gave positive reactions in the quantitative cardiolipin test were treated with penicillin as well as sulphones for their leprosy. The subsequent serological pattern in these cases was that of non-leprous syphilitic patients. It is concluded that the quantitative cardiolipin test is a reliable criterion of syphilitic infection even in individuals with concurrent leprosy.

R. R. Willcox

386. **The Behaviour of the Antilipid and Specific Anti-treponemal Antibodies after Penicillin Treatment.** (Osservazioni sul comportamento degli anticorpi antilipoidale e treponemo-specifico dopo terapia penicillinica)

G. MONTILLI. *Annali italiani di dermatologia e sifilografia* [*Ann. ital. Derm. Sif.*] **9**, 458–463, Nov.–Dec. 1954. 33 refs.

It is known that the adsorption of syphilitic serum with lipoid antigen renders the Wassermann reaction negative but does not prevent a positive reaction to treponemal antigen. Adsorption with treponemal antigen, however, renders syphilitic serum inactive to both tests. These facts led the author, working at the University of Naples, to investigate the behaviour of the antilipoid and the antitreponemal antibodies in 20 cases of syphilis after administration of 6 mega units of depot penicillin given in doses of 1·2 mega units at 4-day intervals. The technique of antilipoid antibody adsorption, which is described, consists essentially in incubation and agitation of the serum with a kaolin–beef-heart suspension.

In 3 out of 6 cases of primary syphilis an initially low titre of antitreponemal antibody disappeared in 24 days after treatment; in the other 3 cases an initially high titre persisted for 2 to 3 months. In 5 of the 6 cases the antilipoid antibody remained unchanged at the end of treatment and disappeared in over 30 days. In 9 out of 14 cases of secondary syphilis the antilipoid antibody disappeared 30 to 35 days after the end of treatment and in the remaining 5 cases in 60 days, whereas the antitreponemal antibody never disappeared in less than 90 days, and its titre returned nearly to the original level in 2 cases after an initial fall.

The author found that the higher the initial titre, the more slowly did it disappear. The occurrence of some degree of oscillation of the two titres during penicillin therapy is explained on the hypothesis that the reticulohistiocytic system has a limited capacity to produce antibody. The return of the antitreponemal antibody after a course of 6 mega units of penicillin is in contrast to the usual complete disappearance of this antibody after treatment with arsenobenzol and bismuth, and the author suggests therefore that lipoid and treponemal antigens should both be used in routine tests as a means of assessing the therapeutic efficacy of the newer antibiotics. *F. Hillman*

387. **The Intradermal Reaction to Treponemal Protein Antigen in Syphilis.** (La intradermoreazione con antigene treponemico proteico nei luetici)
U. MARAGNANI. *Minerva dermatologica* [*Minerva derm. (Torino)*] **30**, 16–22, Jan., 1955. 43 refs.

The intradermal reaction to treponemal protein antigen depends both on individual factors in the patient and on certain factors inherent in the antigen used, such as the mode of preparation and the strain of treponema. Figures quoted from the highly controversial literature show that positive reactions have been obtained in 0 to 25% of cases of primary and secondary syphilis, in 70 to 100% of tertiary syphilis, and in 30 to 100% of congenital cases, suggesting that the test is not diagnostic at any stage of the disease.

Using Reiter's treponema, the antigenic structure of which is discussed, the author, working at the Civil Hospital, Alessandria, has given 0·1 ml. of a 1-in-100 dilution of protein from this treponema by intracutaneous injection to 110 syphilitic patients and a number of control subjects. A strong positive response was obtained in only 3 cases of late latent syphilis, in one of general paresis, and one of congenital syphilis; weak reactions were obtained in another 8 cases and doubtful reactions in 13. No reaction was noted in the remaining 84 cases or in the controls. All 5 patients giving a strong positive reaction also reacted to another non-specific skin test, and one of the patients reacted very strongly to all of 4 non-specific skin tests. Attempts to produce passive transfer of allergy by injecting serum from reacting patients together with antigen into weak reactors gave inconclusive results, and injection of blister fluid from these patients mixed with antigen gave negative results. Antihistaminic drugs did not influence the results, but hyaluronidase was found to diminish the response by shortening the time of contact between antigen and antibody. Titration of the antigen in an attempt to construct an allergometric curve was unsuccessful, since further dilution rendered the results doubtful.

The author suggests that variation in results between different series may be due to differences in interpretation or in the antigen preparation employed. Reiter's treponema gives a lipoid, a thermolabile protein, and a heat-stable polysaccharide antigen, and the last-named might be more suitable for skin tests. On the whole the author considers that his poor results were mainly due to the nature of the antigen used. *F. Hillman*

388. **The Serum Protein Picture in Syphilis.** (Il quadro sieroproteico nella sifilide)
G. POZZO and M. F. HOFMANN. *Giornale italiano di dermatologia e sifilologia* [*G. ital. Derm. Sif.*] **95**, 569–610, Nov.–Dec., 1954. 6 figs., 37 refs.

This discussion of changes in the serum protein picture in syphilis is presented from the Dermatological Clinic, University of Milan. The authors consider that there occurs in syphilis a disturbance of the globulino-poietic mesenchyme, and that the results of a whole group of reactions (the *Reaktions-Konstellationen* of Wuhrmann and Wunderly) should be considered in relation to the stage of the disease. The following tests were carried out on 32 patients in all stages of syphilitic infection and on 10 with non-specific reactions: determination of total serum protein content biochemically and by paper electrophoresis, analysis of euglobulins (the Boselli reaction), and the colloidal tests of MacLagan and Kunkel.

Briefly, they showed that in 3 seronegative cases of primary syphilis the serum protein pattern and the colloid state were normal. In 3 seropositive cases of primary syphilis and 4 of secondary syphilis there was a mild decrease in albumin content with an increase in α and γ globulins and a disturbance in the flocculation reactions. In 10 seropositive cases of latent or cured syphilis there was a very slight increase in the α-euglobulin and γ-pseudoglobulin values, while a number of cases of "cured" congenital and acquired syphilis showed normal values. Lastly, 6 cases in which a Herxheimer reaction occufred were analysed. In one of these patients, who was seronegative and had a chancre, a normal serum protein picture was present; the others showed mild irregularities within the margin of error of the method.

The problem of the biological false positive Wassermann reaction is considered in detail. The authors suggest that it may be due (1) to an antibody, such as occurs in yaws or bejel, (2) to some alteration in the serum globulins, or (3) to a change in the chemical constituents of the blood [but this last group is not further considered]. In support of the first they cite 10 cases of leprosy showing a marked increase in the γ-globulin (mainly euglobulin) value and intensely positive flocculation reactions; in other cases, not associated with any special disease, there may be a mild hypo-albuminaemia with increase of α_2-euglobulin or pseudoglobulin value, and also an increase in γ-euglobulin content. It is sug-

gested that the last-mentioned is of value in differentiating between biological false positive results and those in cases of latent or congenital syphilis. *F. Hillman*

389. **A Note on the Specificity of Cardiolipin and Standard Antigens in Testing Sera for Syphilis**
I. N. O. PRICE. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **30**, 210–211, Dec., 1954. 4 refs.

Previous work by the author on the relative sensitivity of cardiolipin and standard antigens in the Wassermann reaction is reviewed, from which it was concluded that "cardiolipin antigen gave more non-treponemal reactions than standard antigens when routine sera were tested". The present communication describes the reinvestigation of this question by the parallel testing with the two antigens of sera which had given anomalous results on routine testing.

Of 8,750 such "problem sera" referred to the V.D. Reference Laboratory, St. Peter's Hospital, London, for opinion, 1·92% gave non-treponemal reactions with cardiolipin antigen compared with 1·69% with standard antigen when the Whitechapel Wassermann technique was used. In precipitation tests, 6·2% of 1,886 problem sera gave non-treponemal reactions with cardiolipin antigen (V.D.R.L., Chamblee), and 0·57% with the standard antigen used in Price's precipitation reaction (P.P.R.). Of 3,097 routine sera, 2% gave non-treponemal reactions in the V.D.R.L. test and 0·2% with the P.P.R. Of the sera from cases of treated syphilis in each of the same three series, where there was any discrepancy in the results, those cases in which the cardiolipin antigens gave positive results and the standard antigens negative were about 20 times more frequent than those in which the standard antigens gave positive results and the cardiolipin antigens negative.

It is thus concluded once more that the more sensitive cardiolipin antigens are more liable to give non-treponemal reactions than the standard antigens consisting of unpurified alcoholic extracts of ox heart.

P. J. L. Sequeira

390. **Use of the Price Precipitation Reaction in Northern Rhodesia**
A. J. EVANS. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **30**, 212–213, Dec., 1954. 5 refs.

Conditions in Northern Rhodesia, where specimens for serological testing often have to be sent long distances in adverse climatic conditions, are described and the need for a simple, robust test for syphilis for use in tropical areas is stressed. The result of Price's precipitation reaction (P.P.R.) in 200 selected cases in which the results of the Kahn test and a slide modification of the Rappaport test were in agreement with the clinical findings are reported. The P.P.R. antigen was brought from England by sea and land, kept for a year at laboratory temperature, and used at the hottest time of the year, 1 to 3 months after its official expiry date. The Kahn antigen was obtained by air from Johannesburg and used for preparation of the Rappaport antigen.

There were no major disagreements between the results except in one case of untreated syphilis of one year's duration, in which the Kahn and Rappaport tests gave strongly positive results and the P.P.R. negative. This result was thought to be due to a zone phenomenon. The P.P.R. appeared to be slightly less sensitive than the Kahn test in primary syphilis, but was more sensitive than the Rappaport test.

It is concluded that the P.P.R. works satisfactorily, and that its antigen is stable, under tropical conditions.

[Zone phenomena are liable to occur in all one-tube precipitation tests. If the P.P.R. is used alone, the inclusion of a second tube with a serum dilution of about 1 in 8 or 1 in 16 should serve to detect all zones.]

P. J. L. Sequeira

391. **Malaria Therapy in Neurosyphilis.** (La malarioterapia nei neuroluetici)
P. M. CARRESCIA and E. MASDEA. *Rivista di malariologia* [*Riv. Malar.*] **33**, 247–260, Dec., 1954. 15 refs.

At the Institute of Malariology, Rome, a total of 506 patients, 397 male and 109 female, with neurosyphilis received malaria therapy between 1936 and 1954. The incidence of general paralysis was significantly higher in the males and of congenital syphilis in the females. In both sexes paralytic forms were commoner than tabetic forms, and the highest incidence for males occurred in the 4th decade and for females in the 5th. The time of onset of neurological symptoms varied widely, but in cases of general paralysis they most frequently developed 16 to 20 years after the primary infection; in the case of tabes there was no peak distribution and symptoms appeared from 5 to 50 years after the primary infection. Most of the patients were given malarial treatment within one year of the appearance of neurological symptoms, only active tuberculosis and decompensated heart disease being regarded as contra-indications. Of the 506 patients 456 were infected by the injection of 7 or 8 ml. of citrated malarial blood intravenously and 50 by the injection of sporozoites. The strains employed were *Plasmodium vivax*, *P. falciparum*, and *P. malariae*.

The incubation period for *P. vivax* was usually less than 5 days when whole blood was given and 23 days when sporozoites were injected. The fever of initial invasion was more commonly seen in cases with the shorter incubation periods, and it never occurred in patients who gave a history of previous malarial infection. In infections with *P. malariae* the peak blood invasion occurred up to the 10th day, and initial fever occurred less frequently than in re-infected patients, whose peak appeared between the 11th and 20th days. The corresponding data are also given for *P. falciparum* infections. The total mortality was 4%, 15 patients dying from benign tertian malaria, one from quartan malaria, and 4 from malignant tertian malaria; the blood in all these cases was free from parasites at the time of death.

The therapeutic efficacy of quinine, chloroquine, "atebrin" (mepacrine), and "paludrine" (proguanil) is assessed in a table [but the effects of malaria therapy on the neurosyphilitic condition are dismissed with the statement that "many cases derived notable benefit"].

F. Hillman

Tropical Medicine

392. **The Clinical Picture of Veno-occlusive Disease of the Liver in Jamaican Children**
D. B. JELLIFFE, G. BRAS, and K. L. STUART. *Annals of Tropical Medicine and Parasitology* [*Ann. trop. Med. Parasit.*], 48, 386–396, Dec., 1954. 5 figs., 23 refs.

Writing from University College of the West Indies, the authors describe the findings in 11 cases of hepatic veno-occlusive disease in Jamaican children. Liver biopsy was carried out in all cases. Three overlapping clinical stages are described. (1) An acute stage, occurring in infants aged from 18 months to 3 years and characterized by sudden hepatic enlargement, often acute ascites, and abnormal results of liver function tests. There may be complete recovery, rapid death from cholaemia, or passage into the subacute or chronic stages. (2) Subacute veno-occlusive disease, characterized by firm hepatic enlargement with or without recurrent ascites and sometimes accompanied by splenomegaly. There is little evidence of a collateral circulation. (3) The chronic stage, in which the picture is identical with that of hepatic cirrhosis, requiring histological examination for positive diagnosis.

A brief account of the histology is given, the condition being primarily a widespread endophlebitis of the smaller branches of the hepatic vein followed by occlusion and a non-portal type of cirrhosis. The aetiology is unknown, but the disease does not appear to be primarily nutritional and the possibility that it is caused by a bacterial toxin is considered. Points of similarity are noted between veno-occlusive disease and serous hepatosis, Chiari's syndrome, senecio poisoning, and Indian infantile cirrhosis.

J. L. Markson

393. **Histopathology of the Pancreas in Jamaican Infants and Children.** [In English]
G. BRAS and K. P. CLEARKIN. *Documenta de medicina geographica et tropica* [*Docum. Med. geogr. trop. (Amst.)*] 6, 327–330, Dec., 1954. 1 fig., 7 refs.

The findings at 49 consecutive necropsies carried out on Jamaican children under 11 years of age were analysed; 16 of them had kwashiorkor-like marasmus and the remainder had miscellaneous conditions, the object of the investigation being to ascertain the relative incidence of histopathological changes in the pancreas in the two groups. The pancreatic lesions observed were atrophy, degranulation of the acinar cells, dilatation of the ducts, increase in intercalated ducts, diffuse fibrosis, and retarded development; metaplasia of the ducts was not seen.

In 3 of the 16 cases of kwashiorkor there were no changes in the pancreas; in the remainder the commonest lesion was diminution or total lack of zymogen granules, followed by atrophy, fibrosis, and a preponderance of intercalated ducts. In 22 of the 33 miscellaneous cases necropsy revealed a fatty liver, and in 15 of these there were lesions in the pancreas; of the 11 cases without fatty change in the liver, only 2 showed pancreatic lesions. There was thus a high degree of correlation between the incidence of fatty change in the liver and the presence of pancreatic disease. The fat in the liver in the miscellaneous cases was widely distributed and not peripheral only, as in kwashiorkor. Comparison of the height and weight of all the children under 2 years of age revealed no statistical difference between the two groups.

The authors consider that their findings do not support the view that the fatty changes in the liver in the miscellaneous cases indicate pre-clinical kwashiorkor.

B. G. Maegraith

394. **Salmonellosis in Jamaican Children.** [In English]
D. B. JELLIFFE, L. E. WYNTER-WEDDERBURN, V. M. YOUNG, L. S. GRANT, and F. H. CASELITZ. *Documenta de medicina geographica et tropica* [*Docum. Med. geogr. trop. (Amst.)*] 6, 315–326, Dec., 1954. 3 figs., 45 refs.

The literature on the incidence and epidemiology of *Salmonella* infections, excluding typhoid and paratyphoid fevers, is reviewed and 40 cases of salmonellosis (acute gastroenteritis in 20, chronic relapsing gastroenteritis in 18, salmonella fever in 1, and meningitis in 1) occurring in poor-class Jamaican children of predominantly African extraction are discussed.

Of the 20 patients with acute gastroenteritis, the average age of whom was 10 months, half were still breast-fed and the majority were poorly nourished. Salmonellae were recovered from the stools, the commonest being *Salmonella typhimurium* and *S. oranienburg*. Treatment consisted in administration of glucose–saline by mouth, with fluid parenterally if necessary, and gradual enrichment of the diet by the addition of half-cream milk. Chloramphenicol in a dosage of 50 mg. per kg. body weight daily or aureomycin in a dosage of 25 to 50 mg. per kg. daily was given for 5 to 7 days. In a few cases sulphonamides were given. Some improvement resulted from this treatment, but relapses were common. The mortality in this group was 10%.

Of the children suffering from chronic relapsing gastroenteritis (average age 9 months) all were underweight and malnourished and passing 3 to 8 semi-solid, mucoid, and sometimes blood-stained stools a day. There was marked anorexia, with persistent vomiting and fever. The illness lasted 5 to 7 days and recurred at intervals of a few weeks. The commonest organism recovered from the stools was *S. typhimurium*. The clinical condition responded to administration of chloramphenicol, oxytetracycline, or aureomycin, but relapses were frequent. Mortality in this group was 28%.

The clinical features of the case of salmonella fever were suggestive of typhoid fever. The response to chloramphenicol in a dosage of 50 mg. per kg. daily for 7 days was rapid and permanent.

The authors emphasize that *Salmonella* infection is a common cause of febrile diarrhoea in infants.

B. G. Maegraith

395. ***Mycobacterium leprae* in Skin and Nasal Scrapings during Sulfone Treatment. A Review of 146 Cases**
J. L. BYERS and R. R. WOLCOTT. *International Journal of Leprosy* [*Int. J. Leprosy*] **22**, 285–287, July–Sept., 1954. 2 figs., 1 ref.

The results of skin and nasal scrapings are recorded in 146 cases of leprosy during periods of sulfone therapy ranging from 6 to 10 years. The nasal mucosa is apparently freed of *M. leprae* in more than 50% of cases within one year of sulfone treatment. The skin is apparently freed of *M. leprae*, as shown by routine skin scrapings, in less than 10% of cases in from 1 to 11 years of sulfone treatment.—[Authors' summary.]

396. **First Report on the Treatment of Sleeping Sickness with Puromycin**
C. TRINCÃO, A. FRANCO, A. NOGUEIRA, A. R. PINTO, and H. MÜHLPFORDT. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **4**, 13–17, Jan., 1955. 7 refs.

A new antibiotic, "puromycin", obtained from *Streptomyces albo-niger*, was administered to 15 natives of Portuguese Guinea suffering from trypanosomiasis due to *Trypanosoma gambiense*, for which no treatment had previously been given; in 7 of these patients there were changes in the cerebrospinal fluid. Capsules containing 0·25 g. of the antibiotic were given by mouth over a period of 7 to 10 days, the maximum daily dose ranging from 1·0 to 2·25 g. In all cases trypanosomes disappeared from the lymph nodes within 48 hours of administration of the first dose, and blood culture was negative in 24 to 72 hours. One patient relapsed 10 days and another 60 days after treatment; in both these cases the total dosage was only 9·5 to 11 g. In 2 further patients a relapse occurred 6 months after treatment, the total dosages being 9·5 g. and 13·5 g. respectively. In these 4 cases of relapse there were changes in the cerebrospinal fluid before treatment. The remaining patients appeared to be free from infection 6 months after completion of the course of puromycin. Toxic reactions included occasional headache, nausea and vomiting, and, in some cases, troublesome diarrhoea. *F. Hawking*

See also Pathology, Abstract 303.

397. **Njovera**
R. R. WILLCOX. *Central African Journal of Medicine* [*Centr. Afr. J. Med.*] **1**, 30–33, Jan., 1955. 5 figs., 15 refs.

The condition known as "njovera", which occurs in the native population of certain areas of Southern Rhodesia, is considered to be a form of endemic syphilis comparable with bejel and other extravenereal treponematoses. Secondary manifestations — condylomata, mucous patches, laryngitis, and bone pains—are generally the first evidence of the disease, generalized eruptions being uncommon. The late lesions are generally of gummatous type, affecting commonly the palate and nasal septum (gangosa), skin, and bones, but the possibility of involvement of the cardiovascular and nervous systems is not ruled out. It is suggested that the gummatous stage may be the result of superinfection in sensitized individuals. *R. Crawford*

398. **Treatment of Schistosomiasis with "Nilodin"**
B. A. KING. *British Medical Journal* [*Brit. med. J.*] **1**, 185–188, Jan. 22, 1955. 2 refs.

Lucanthone hydrochloride ("nilodin") was tried in the treatment of urinary schistosomiasis due to infection with *Schistosoma haematobium* in workers in the mines in the Witwatersrand and Orange Free State; these are "clean" areas, but the labour force is drawn from heavily infested areas. One group of 24 patients received 20 mg. of lucanthone per kg. body weight daily for 12 days. Of 15 followed up for 6 months, 9 were "cured". Toxic symptoms were observed in just over half the patients, but were not severe enough to call for cessation of treatment. Although there was no evidence of albuminuria, toxicity was more severe in patients with impaired renal function. Loss of weight, which was noted in almost two-thirds of the patients, was accompanied in some instances by a marked diuresis. A second group of 22 patients received 25 mg. per kg. body weight daily for 9 days, and of 18 followed up for 6 months, 6 were "cured". Lucanthone was also given to 4 patients with rectal schistosomiasis (*S. mansoni*); there was no clinical evidence of relapse in these 4 cases, but in 2 viable ova were recovered from the rectum.

The author concludes that lucanthone is effective and cheap and the clinical response excellent, but that at least 12 days' treatment is necessary and patients should be followed up for 6 months. *J. L. Markson*

399. **Recent Experiments on Possible Resistance to DDT by *Anopheles albimanus* in Panama**
H. TRAPIDO. *Bulletin of the World Health Organization* [*Bull. Wld Hlth Org.*] **11**, 885–889, 1954. 7 refs.

Experiments were devised and carried out at the Gorgas Memorial Laboratory, Panama, to determine whether, as the result of the intensive use of DDT over a number of years, *Anopheles albimanus* had become resistant to this insecticide.

Blood-engorged females of the species were taken from (1) a stock colony which had never been in contact with DDT or any other chlorinated-hydrocarbon insecticide, (2) a stock-colony strain which had been exposed to DDT for over 70 generations, and (3) two villages in Panama in which 5% DDT in kerosene had been frequently used; all were then exposed for 12 minutes to 0·5% DDT in mineral oil. After 24 hours the percentages of dead mosquitoes in the three groups were 92, 85, and 96 respectively. Under the conditions of the investigation, which was carefully controlled, there appeared to be no resistance to DDT, and the author concludes that any difference in its effectiveness for *A. albimanus* must be "due to a behaviour change rather than to any change in the intrinsic toxicity of DDT for the mosquito". *W. H. Horner Andrews*

Allergy

400. The Effects of Drugs upon a Graded Cough Response Obtained in Sensitized Guinea Pigs Exposed to Aerosol of Specific Antigen

C. A. WINTER and L. FLATAKER. *Journal of Experimental Medicine* [*J. exp. Med.*] **101**, 17–24, Jan. 1, 1955. 7 refs.

Studies carried out at the Institute for Therapeutic Research, Rahway, New Jersey, in which the production of passive sensitization of guinea-pigs with known amounts of antibody was combined with recording of the latent period and number of coughs excited by an aerosol of the specific antigen in 10 minutes, have enabled more precise investigation to be made of the effect of drugs on this antigen–antibody reaction. Guinea-pigs sensitized with 80 μg. of antibody nitrogen contained in rabbit antiserum against bovine plasma albumin gave a maximal cough response to antigen aerosols in concentrations of 0·02% or higher. A linear relationship between the number of coughs and the dose of antibody nitrogen used for sensitization was established for doses between 20 and 80 μg.

Codeine, morphine, " propadrine " (phenylpropanolamine), and narcotine, which were effective in reducing the cough response to simple irritants, were ineffective against the antigen aerosol. On the other hand, antihistaminic drugs and cortisone, which were ineffective against simple irritants, were effective in increasing the latent period before coughing began and in reducing the number of coughs after administration of the antigen aerosol, the antihistaminic drugs " phenergan " (promethazine hydrochloride) and mepyramine maleate being more effective than cortisone. A combination of these drugs with cortisone showed a synergistic action, and resulted in almost complete suppression of the reaction to the aerosol of the antigen. *J. Pepys*

401. Studies in Sensitization as Applied to Skin Testing Procedures. II. Influence of Allergen Contact

L. TUFT and V. M. HECK. *Journal of Allergy* [*J. Allergy*] **26**, 59–70, Jan., 1955. 14 refs.

To determine the importance of contact with allergens in the production of sensitization in allergic individuals which causes the occurrence of positive skin-test reactions having little apparent clinical significance, case histories of over 600 patients were studied. The reactions to horse serum and horse hair in the routine test were noted in each case and the history reviewed for evidence of possible previous contact with horse serum or horse hair, while the skin reactions to a number of commonly and uncommonly eaten foods were similarly noted and the patient's eating habits determined. Wherever possible, information contained in the case history was supplemented by interrogation of the patient. It was found that those patients who had been given injections of horse serum in the past very frequently gave positive skin reactions to horse serum and to horse hair, although there was no clinical allergy to these substances. It was also found that skin reactions to foodstuffs eaten frequently were more often positive than those to foodstuffs seldom eaten. In comparative tests on 100 allergic and 100 non-allergic subjects the allergic subjects gave a positive reaction to the former much more often than the non-allergic, though with rarely eaten foods this difference was not so pronounced [but the total number of positive reactions to this group of foods was much smaller]. The authors conclude that in many cases a positive skin reaction is explained by previous contact with the allergen and is of no clinical importance. Sensitization, once induced, may persist for a very long time without further contact with the allergen.

H. Herxheimer

402. An Interpretation of the Results of Skin Testing in Seasonal Pollinosis

D. A. PRENTICE. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 308–314, Feb. 26, 1955. 14 refs.

The results of skin tests with various grass pollens on patients suffering from seasonal pollinosis are analysed. The tests were carried out at St. Vincent's Hospital, Melbourne, with 16 different species of subfamilies of *Gramineae*. There was a marked skin reaction to the tests in 85% of the patients, a slight positive response in 8%, and no reaction in 7%. The results were similar for each individual grass subfamily and for individual species. It is suggested that these pollens have common as well as specific antigenic components, and that a classification of the grasses on the basis of antigenic relationships might be entirely different from that based on morphological characteristics. *A. W. Frankland*

403. Skin Reactions in Atopic Eczema

R. H. MEARA. *British Journal of Dermatology* [*Brit. J. Derm.*] **67**, 60–64, Feb., 1955. 3 figs., 3 refs.

At St. John's Hospital for Diseases of the Skin, London, the reactions to skin tests of 112 children suffering from infantile eczema and Besnier's prurigo were compared with those of 43 children suffering from other skin diseases. The scratch method was employed with standard skin-testing extracts.

Of the 112 children with eczema, 73 gave positive reactions, while all the control group gave negative reactions. The incidence of positive reactions increased with age, 90% of children over 7 years of age reacting to one or more of the test substances. Reactions to egg were most frequent in children under 2 years, while the reverse was the case with pollens. Positive reactions were obtained with all the food substances tested, but to very few of the textiles or inhalants other than pollens. When the tests were repeated after an interval of 6 months the reactions were " virtually identical " in 80% of the children.

There was a history of asthma in 19 of the patients with eczema, and in all 19 a positive reaction to either pollen

or egg was obtained. When egg was omitted from the diet of 29 egg-sensitive children the eczema was not affected, although 8 of those children developed urticarial reactions within a few minutes of resuming consumption of eggs.

The author concludes that the results of skin testing may be of diagnostic significance, but have no prognostic value. *Elaine M. Osborne*

404. **Seasonal Hay Fever and Asthma Treated with Pollen Extracts**
A. W. FRANKLAND. *International Archives of Allergy and Applied Immunology* [*Int. Arch. Allergy*] **6**, 45–52, 1955. 12 refs.

At the Wright–Fleming Institute Allergy Clinic, St. Mary's Hospital, London, the author compared the effect of individual grass pollens and a combination of two such pollens in the treatment of 200 pollen-sensitive patients. The patients were divided at random into 4 groups, each of 50 patients, the groups receiving respectively pollen extracts of the following grasses: (1) timothy, (2) fescue, (3) cocksfoot, and (4) cocksfoot with timothy. The groups were comparable as regards age at onset of symptoms and at the time of treatment, and each included approximately the same number of patients with pollen asthma (20 to 26). Only 2 to 4 patients in each group defaulted before an adequate dose of pollen had been given.

The results of treatment, assessed as "good", "moderate", or "poor", were about the same for all 4 pollens. Approximately 70% of good results and 10% of poor results were obtained in the patients with hay-fever, the percentages for the patients with pollen asthma being 80 and 6. This investigation thus showed that although individual specificity has been demonstrated for different grass pollens in addition to a common antigenic property, equally good results were obtained by desensitization with one of these separate pollen extracts and with a combination of two.

R. S. Bruce Pearson

405. **Hydrocortisone Tablets in the Treatment of Asthma with Persistent Dyspnoea.** (Le traitement des asthmes à dyspnée continue par l'hydrocortisone en comprimés)
J. TURIAF, P. MARLAND, and Y. JEANJEAN. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **70**, 966–975, Oct. 29, 1954. 1 fig., 10 refs.

The authors report excellent results from the treatment with cortisone of chronic asthma accompanied by persistent dyspnoea. In 11 such cases, however, the use of hydrocortisone acetate had to be discontinued because it caused severe water retention. Thereafter 48 patients with severe asthma were treated with hydrocortisone free alcohol in an initial dose of 100 mg. per day, decreasing to 30 to 60 mg. daily as a maintenance dose. The patients were kept on a low-sodium diet and received 1·5 to 2 g. of potassium chloride daily and one injection of 40 to 50 mg. of testosterone per week. (The authors consider that testosterone protects the adrenal glands against atrophy.) The doses of hydrocortisone necessary to suppress asthmatic attacks were lower than those of cortisone, and the compound was better tolerated. In many cases hydrocortisone caused polyuria, but in spite of this an increase of body weight was observed.

Kate Maunsell

406. **The Influence of Bile and Bile Acids on Experimental Anaphylaxis and Allergic Diseases.** (О влиянии желчи и желчных кислот на экспериментальную анафилаксию и аллергические заболевания)
R. KADLUBOVSKI. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **33**, 77–79, Jan., 1955. 8 refs.

Some 4 years ago the author and his co-workers noticed that a patient with severe bronchial asthma experienced great relief from his symptoms during an attack of jaundice. Other authors have also reported similar observations. Experiments on guinea-pigs showed that animals given intracardial injections of bile (1 ml. per kg. body weight) 16 days after sensitization to horse serum withstood anaphylactic shock, 13 out of 15 animals surviving, whereas all of 10 controls died. In another series of experiments cholic acid in doses of 5 mg. per kg. body weight was injected; out of 10 guinea-pigs given horse serum after sensitization, 7 developed no shock. Lastly, repeated intraperitoneal injections of dehydrocholic acid (10 mg. per kg.) were effective in inhibiting histamine shock.

Following these experiments, dehydrocholic acid was used in the treatment of 9 cases of bronchial asthma and 3 cases of urticaria, all of which had been resistant to other forms of treatment; improvement was noted after 3 to 10 injections. The acid was given as an intravenous injection of 0·5 g. in a 5% solution and repeated every other day; if improvement resulted, the injections were continued at a rate of one or two a week. Successful results were also obtained in migraine and neurodermatitis, but similar treatment in cases of hay-fever and Quincke's disease (angioneurotic oedema) was ineffective. The mechanism of this desensitizing effect of bile is still obscure—the action may be upon the nervous system, the liver, or the adrenal glands, or the bile may act purely as a spasmolytic. The author suggests that as an attack of jaundice is known to relieve rheumatoid arthritis, the treatment might be tried in this condition also. *L. Firman-Edwards*

407. **The Use of Hydrocortisone Suspension in Nasal Allergic and Infectious Conditions**
M. B. ROHEN. *Annals of Allergy* [*Ann. Allergy*] **13**, 109–114, Jan.–Feb., 1955. 5 refs.

Topical application of a hydrocortisone suspension was tried at the Gouverneur Hospital, New York, in the treatment of 8 patients with chronic allergic rhinitis, some of whom also had a superimposed acute upper respiratory tract infection. The suspension contained 20 mg. of hydrocortisone per ml. of normal saline solution, and 3 to 5 drops were instilled into each nostril 3 times a day. In all cases there was marked improvement or complete relief of symptoms. No side-effects were observed. *H. Herxheimer*

Nutrition and Metabolism

408. Studies in Calcium Metabolism. Effect of Food Phytates on Calcium^{45} Uptake in Children on Low-calcium Breakfasts

F. BRONNER, R. S. HARRIS, C. J. MALETSKOS, and C. E. BENDA. *Journal of Nutrition* [*J. Nutr.*] **54**, 523–542, Dec. 10, 1954. 22 refs.

In a study carried out at Harvard Medical School, Boston, by the "one-meal technique" 19 adolescent boys in an institution were given a low-calcium breakfast consisting of (1) a phytate-rich cereal (oatmeal), (2) a phytate-free cereal ("farina"), or (3) farina and sodium phytate. The amounts of calcium, mainly as milk, in the 3 meals were 91, 83, and 83 mg. and of phytate phosphorus 116, 0, and 78 mg. respectively. At the same time all three groups received 0·85 μc. of radioactive calcium (^{45}Ca), calcium uptake being then assessed by estimation of ^{45}Ca in the serum, urine, and faeces for 5 days. Each subject took two of these meals, with an interval of 30 days between.

It was shown that the calcium uptake from the phytate-rich oatmeal breakfast was 74%, and that from the farina-plus-phytate breakfast 45%, of that from the phytate-free farina. It was thus evident that significantly less ^{45}Ca was taken up in the presence of sodium phytate than in the presence of an equivalent amount of phytate phosphorus supplied by the oatmeal. *A. C. Frazer*

409. Effects of Diet on Blood Lipids in Man. Particularly Cholesterol and Lipoproteins

A. KEYS, J. T. ANDERSON, F. FIDANZA, M. H. KEYS, and B. SWAHN. *Clinical Chemistry* [*Clin. Chem.*] **1**, 34–52, Feb., 1955. 2 figs., bibliography.

In this paper from the University of Minnesota, Minneapolis, the authors summarize the results of a large number of systematic studies of the influence of diet on the blood lipid level in man which have been carried out in the U.S.A. and various countries in Europe and Africa during the past 6 years on different social and racial groups, entailing rigid nutritional surveys, exact laboratory tests, and detailed statistical evaluation.

These studies have confirmed that, in contrast to the findings in some experimental animals, the amount of dietary cholesterol has little or no influence on the blood cholesterol level in man. The latter, however, is markedly affected by the total fat content of the diet. The influence of the total caloric intake *per se* on blood lipid levels is slight and is dependent mainly on individual differences in fat metabolism, but the proportion of calories supplied by fat in the diet is important. For example, the average serum cholesterol level in men in countries where the dietary fat provides 35 to 40% of the total caloric intake, as in the U.S.A., Great Britain, and Sweden, is 25 to 50% higher than in men in countries where the dietary fat provides only about 20% of the total caloric intake, as in certain parts of Italy and Spain. At the age of 25 the mean serum cholesterol level among populations living on high-fat diets is about 50 mg. per 100 ml. higher than in those on low-fat diets, but whereas this value rises regularly in the former to 75 mg. per 100 ml. at about the age of 50, no such increase in the serum cholesterol level with age occurs in the latter. A similar relationship holds good for the beta-lipoprotein fraction, which carries about 75% of the total cholesterol.

A reduction or increase in the dietary fat level has a noticeable influence on the serum cholesterol concentration within a few weeks, but eventually a new constant level is arrived at and later changes are very slow. The most marked differences appear when a comparison is made between populations or social classes subsisting habitually on diets with widely differing fat contents. The complex mechanism by which the amount of fat in the diet controls the qualitative and quantitative composition of the blood lipids is at present unknown.

[This is an important paper. It is now generally acknowledged that a significant relationship exists between the concentration of certain blood lipids and the development of coronary atherosclerosis, and that the nature of this relationship urgently requires clarification. It is the authors' intention that the ultimate conclusions from this world-wide concerted study shall be formulated from the pooled data of many investigators, but it may take up to two years before these can be published.] *Z. A. Leitner*

410. Fat Excretion. The Influence of Dietary Fat on Fecal Fat Excretion

L. N. NORCIA and W. O. LUNDBERG. *Journal of Nutrition* [*J. Nutr.*] **54**, 491–508, Dec. 10, 1954. 1 fig., 11 refs.

In a study of the influence of dietary fat on the excretion of fat in the faeces two groups of 25 rats were fed for 30 days on diets containing, as the only lipid, 15% of tripalmitin and 15% of olive oil respectively. These were then divided into five sub-groups of 5 rats each. One sub-group was killed at once and the body fats analysed; the other 4 sub-groups were fed on four test diets for 10 days, one being fat-free, one containing tripalmitin, one triolein, and the fourth equal parts of tripalmitin and trilinolein.

It was shown that the amount of endogenous faecal fat was unaffected by the quantity or composition of the fat in the diet, but there was a definitely increased loss of unabsorbed dietary fat in animals receiving the tripalmitin diet. Although the composition of the depot fats was markedly different in the animals receiving the various diets, this had no demonstrable effect on the composition of the faecal fat. It is concluded that non-dietary faecal fat is synthesized by intestinal bacteria and is not secreted into the lumen of the intestine or derived from desquamated intestinal mucosal cells.

A. C. Frazer

Gastroenterology

411. **Oesophageal Reflux**
B. CREAMER. *Lancet* [*Lancet*] **1**, 279–281, Feb. 5, 1955. 5 figs., 1 ref.

At St. Thomas's Hospital, London, the author studied the mechanism of oesophageal reflux by measuring oesophageal and gastric pressures with fine, water-filled, " polythene " tubes in 12 cases of oesophageal reflux (in 8 of which hiatus hernia was present), 12 cases of normal functioning cardia serving as controls. By simultaneous screening of the patient after a barium emulsion had been swallowed it was possible to demonstrate a rise in oesophageal pressure due to reflux, whether of gas or fluid. Reflux occurred only during inspiration, was not constant, and was observed most frequently when the patient leaned forward while sitting in bed; it was next most commonly seen in the supine position. No rise in gastric pressure greater than that due to inspiration preceded reflux, and no appreciable change in the pressure gradient across the cardia was observed. This suggested that reflux was not due to the forcing of fluid back through the cardia. There was no evidence of reflux peristalsis in any of the cases; in many instances reflux initiated a propulsive contraction of the oesophagus which progressed in a normal direction. In some patients with oesophagitis it produced uncoordinated contractions which were localized and non-propulsive; the oesophageal pain in these patients was not related to the contractions. In the patients with hiatus hernia the pressure inside the hernia did not vary directly with that in the oesophagus, and the results are interpreted as indicating that the cardia may be incompetent only at the beginning of inspiration.

The general conclusion is that reflux is produced by anatomical changes at the cardia (increased obtuseness of the angle between the oesophagus and the stomach) rather than by abnormal pressure effects.

T. D. Kellock

412. **Oesophageal Reflux and the Action of Carminatives**
B. CREAMER. *Lancet* [*Lancet*] **1**, 590–592, March 19, 1955. 2 figs., 8 refs.

Oesophageal reflux is common, but its mechanism is obscure. It clearly must depend on some change at the cardia which makes reflux possible, and in an attempt to define this change a search was made for drugs that would produce reflux in healthy subjects. Since the same changes in intragastric pressure take place whether the reflux consists of gas or fluid, the author has investigated the action of carminatives—since these invariably cause eructation—on the cardia of 10 healthy subjects at St. Thomas's Hospital, London. Intra-oesophageal and intragastric pressures were measured through fine " polythene " tubes by Hansen capacitance manometers. In each experiment control observations were made with the subject in various postures to test the competence of the cardia before the administration of carminatives; in all cases the cardia was shown to be competent. After the subject had drunk the carminatives, continuous pressure recordings were made for 15 minutes. A similar study, with the addition of gastroscopic observations, was made on 6 patients undergoing routine investigations for symptoms of dyspepsia; in these cases the carminatives were introduced into the stomach through a fine polythene tube attached to the gastroscope. The carminatives employed were the compound and the aromatic tinctures of cardamom, concentrated oil of dill, and an emulsion of oil of dill in water.

Recordings of the intra-oesophageal and intragastric pressures showed that the carminatives caused oesophageal reflux similar to that seen in pathological states. Gastroscopy revealed that the carminatives produced marked hyperaemia of the gastric mucosa, and it is known from other studies that their effect on the muscularis mucosa is insignificant. The author concludes therefore that it is the hyperaemic mucosa which interferes with the neat closure of the mucosal valve at the cardia and so allows reflux to take place. He suggests that this mechanism may underlie reflux in other conditions in which the pliability of the mucosa is decreased, for example, by the increase in the number of mucosal cells in hypersecretion, infiltration of the mucosa with exudate as in gastritis, or infiltration by neoplastic tissue.

E. Forrai

413. **Differential Diagnosis between Benign and Malignant Gastric Ulcer by Means of a Penicillin Test.** (Дифференциальная диагностика между доброкачественной и раковой язвами желудка при помощи пенициллиновчой пробы)
P. D. TARNOPOLSKAYA. *Советская Медицина* [*Sovetsk. Med.*] No. 2, 36–40, Feb.,1955.

The penicillin test here described was discovered entirely by accident. A patient who was believed to be suffering from malignant gastric ulcer developed a pulmonary infection and for this was treated with injections of penicillin. The immediate improvement in the radiographic appearances and clinical course of the gastric lesion was dramatic; the further evolution of the lesion proved it to be a benign ulcer, which soon healed completely.

In view of this unexpected finding the penicillin test was then applied to 58 patients suffering from gastric ulcer, the antibiotic being given by intramuscular injection in doses of 6 to 10 mega units spread over 7 to 10 days, after which a full radiological examination was carried out. The test showed that the lesion was benign in 45 cases and malignant in the remaining 13. In 18 of the 45 benign cases the ulcer was completely healed within a short time, and in general the response to penicillin was favourable, the infiltration of the edges

of the ulcer completely disappearing in 36 cases, while in the remaining 9 cases it greatly diminished. There was no appreciable response to the penicillin test in any of the 13 patients in whom the ulcer subsequently proved to be malignant. *A. Orley*

414. Results of Partial Gastrectomy in Treatment of Peptic Ulcer
C. D. ANDERSON, R. T. S. GUNN, and J. K. WATT. *British Medical Journal* [*Brit. med. J.*] **1**, 508–511, Feb. 26, 1955. 2 figs., 13 refs.

The value of partial gastrectomy of the Polya type in the treatment of peptic ulcer was assessed from the findings at a follow-up investigation of 481 cases operated on at the Western Infirmary, Glasgow, between 1940 and 1951. Of 481 patients who survived the operation, 23 died from intercurrent disease; of the remainder, 415 (90·6%) were traced. On the authors' criteria the results were good in 64% of these and satisfactory in 24%; direct questioning of the patients, however, revealed that 81% considered the results to be good and 15% considered them satisfactory. No significant difference was observed between the results of antecolic and those of retrocolic anastomosis. There was no correlation between the clinical outcome and such factors as the patient's age, duration of symptoms, and the site of the ulcer. The results were similar in males and females, except that the latter were more liable than males to develop anaemia.

Of the 23 deaths, 8 were due to tuberculosis; in addition, 8 of the survivors had pulmonary tuberculosis, making a percentage incidence for the whole series of 3·3. The authors suggest that this indicates an increased liability to tuberculosis in patients who have undergone partial gastrectomy.

Loss of weight was marked in 29·5% of the males and 49·1% of the females. The authors quote Visick for the view that recurrent ulceration depends on the level of gastric resection. In the present series the level of resection was above the lowest of the vasa brevia and ulceration recurred in only 4 cases (0·9%). At the time of follow-up, which was not less than one year after operation, 11·8% of the patients had severe dumping symptoms or bilious vomiting, or both. Within 6 months of operation 84% of the patients had returned to their former occupation. Moreover, 72·4% of those who worked in heavy industries were able to resume their former employment. *Norman C. Tanner*

415. The Treatment of Parenchymal Diseases of the Liver with Total Liver Extract. (Zur Behandlung von Leberparenchymkrankheiten mit Lebertotalextrakten)
F. LASCH. *Gastroenterologia* [*Gastroenterologia (Basel)*] **82**, 270–284, 1954. 7 figs., 14 refs.

The author describes the treatment of 46 patients with parenchymal hepatic disorders who were observed at the County Hospital, Villach, Austria. In all cases the standard treatment consisted in low-sodium, high-potassium diet, with as much as 300 g. of protein daily, laevulose given by intraduodenal drip when the serum bilirubin level was above 3 mg. per 100 ml., vitamins B and C, and adrenocortical extract. Poultices and short-wave diathermy were also used, with strophanthin, ion-exchange resins, and mercurial diuretics as alternative measures. Liver extract, when given, was in doses of 5 ml. daily intravenously. All the usual liver function tests were performed. In cases of acute hepatitis treatment with liver extract was begun if improvement did not appear after 14 to 20 days of the standard therapy, while if the condition remained unsatisfactory after a further 14 to 20 days surgical exploration was advised.

No numerical results are given for the patients with acute hepatitis, but treatment with liver extract is not recommended in such cases. Of 5 cases of subacute hepatitis, 4 improved, and of 13 of chronic interstitial hepatitis, 10 improved, although normal serum protein values were obtained in only 5. Of 12 cases of cirrhosis of all types (including biliary), 5 improved in respect of diuresis, the clinical picture, and the result of biochemical tests, except those for serum protein values. Of 7 cases of the hepato-renal syndrome, 4 were benefited, and 2 patients with toxic hepatitis secondary to active pulmonary tuberculosis improved while under treatment.

[The details given are few and not very convincing.] *W. A. Bourne*

416. Studies of the Anemia in Ulcerative Colitis with Special Reference to the Iron Metabolism. [In English]
M. BARR, S. DELAVA, and R. ZETTERSTRÖM. *Acta paediatrica* [*Acta paediat. (Uppsala)*] **44**, 62–72, Jan., 1955. 2 figs., 21 refs.

417. Psychophysiological Correlations in Ulcerative Colitis
A. KARUSH, R. B. HIATT, and G. E. DANIELS. *Psychosomatic Medicine* [*Psychosom. Med.*] **17**, 36–56, Jan.–Feb., 1955. 6 figs., 14 refs.

In an investigation carried out at Columbia University College of Physicians and Surgeons, New York, the activity of the colon of 6 patients with chronic ulcerative colitis was studied during a psychiatric interview by means of records of the pressure changes in balloons placed in the sigmoid colon and rectum. The emotion most often associated with contraction of the colon was fear, sometimes conscious but more often unconscious. Fear was aroused by inhibited sexual desire, by rage at frustrating "parentified" authority, or by the real or anticipated loss of the support provided by that authority. Tenesmus was sometimes complained of without there being any accompanying colonic activity. "Activation" of the colon was always associated with emotional excitement, and it subsided with the departure of the psychiatrist, except in one case in which the patient continued to brood about the interview.

[The difficulty in evaluating these interesting observations is to know how much allowance to make for the emotional effect upon the patient of having balloons put into his bowel and being subjected to questions intended to be disturbing. However, all observations on psychological correlation are valuable, and these are the first of their kind to be made on patients with active ulcerative colitis.] *Desmond O'Neill*

Cardiovascular System

418. **Right Ventricular Hypertrophy. I. Correlation of Isolated Right Ventricular Hypertrophy at Autopsy with the Electrocardiographic Findings. II. Correlation of Electrocardiographic Right Ventricular Hypertrophy with the Anatomic Findings**
I. C. WALKER, R. C. SCOTT, and R. A. HELM. *Circulation* [*Circulation* (*N.Y.*)] **11**, 215–222, 223–227, Feb., 1955. 5 figs., 24 refs.

In a search of the records of 4,000 necropsies performed at the Cincinnati General Hospital during the 6 years 1948–53, 22 cases were discovered in which isolated hypertrophy of the right ventricle was present, the criterion being a right ventricular wall 5 mm. thick (or 4 mm. if the ventricle was dilated) combined with a left ventricular wall 13 mm. thick or less. In 16 of the cases no evidence of those conditions, such as rheumatic heart disease, cor pulmonale, and congenital heart disease, usually associated with right ventricular hypertrophy could be found. In none of these 16 were any of the following electrocardiographic criteria of right ventricular hypertrophy present: an S wave in V_5 or V_6 of 7 mm. or more; an R wave in V_1 and an S wave in V_5 or V_6 together amounting to 10·5 mm. or more; or an R : S ratio in V_1 of more than 1; nor were any of these signs present in one of the other cases in which mitral incompetence was diagnosed.

In contrast, of 12 patients with electrocardiographic evidence of right ventricular hypertrophy who were examined post mortem, 8 were shown to have such hypertrophy, while 11 had conditions usually associated with increased right ventricular pressure.

[It seems obvious that, in the absence of a raised pressure in the right ventricle, slight increases in the muscle mass alone will not cause changes in the electrocardiogram.] *C. W. C. Bain*

419. **The Operative Treatment of Cardiac Aneurysm.**
(Die operative Behandlung des Herzaneurysmas)
F. F. NEIDNER. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **80**, 177–179, Feb. 4, 1955. 31 refs.

Cardiac aneurysm occurs most frequently as a complication of myocardial infarction, although an increasing number of cases are being observed nowadays which are the result of cardiac contusion sustained in motor accidents. In the author's experience hypertensive patients and those with infarction not treated by strict bed rest are particularly prone to develop aneurysm. The aneurysmal wall is generally only 1 to 3 mm. thick, but is usually supported by an adherent pericardium. An appreciable proportion of these aneurysms rupture, and the author finds it surprising that little appears to have been written on the operative treatment of this condition.

Working at the Municipal Hospital, Ulm, Württemberg, he has successfully operated on 3 such cases. Direct excision of a ventricular aneurysm was considered not feasible. The normal pericardium was first incised at some distance from the aneurysm; a suitable skin graft from the leg was then stitched to the pericardium, surrounding and slightly compressing the aneurysm; 2 patients have so far been treated in this way. In one case of aneurysm of the auricular wall the aneurysm was excised and the defect closed by suture before applying the graft. All 3 patients tolerated the operation well. The author believes that incision of the pericardium interrupts a pericardio-coronary reflex and thereby is likely to diminish anginal attacks. He suggests also that resection of the pre-aortic plexus might be performed during the same operation in suitable patients. (A more detailed description of the operation is promised in a future communication.) *F. Starer*

420. **The Clinical and Electrocardiographic Differentiation of Supraventricular and Ventricular Tachycardia with Regular Rhythm**
V. SCHRIRE and L. VOGELPOEL. *American Heart Journal* [*Amer. Heart J.*] **49**, 162–187, Feb., 1955. 15 figs., bibliography.

From the University of Cape Town and Groote Schuur Hospital the authors present a detailed survey of 79 cases of paroxysmal tachycardia in order to emphasize the value of auscultation and of examination of the jugular venous pulse in distinguishing between supraventricular and ventricular tachycardia in such cases. Two negative findings may be noted first: (1) pressure on the carotid sinus was found to be of little diagnostic value—and in one case was misleading in that it terminated an attack of ventricular tachycardia; and (2) the slight irregularity sometimes present in ventricular tachycardia was also of little value as it was usually not detectable clinically—moreover, it may occur in cases of auricular tachycardia, particularly auricular flutter.

The major positive conclusion reached is that the differentiation of a supraventricular from a ventricular tachycardia can usually be made by "careful bedside auscultation" if attention is paid to splitting of the heart sounds. It is stated that in a case of rapid regular tachycardia wide splitting of both sounds indicates ventricular tachycardia, whereas if the first and second sounds are single or normally split the tachycardia is supraventricular in origin. If, in addition to wide splitting of both sounds, there is variation in the intensity of the first sound with independent, irregular "Cannon A" waves in the jugular venous pulse, the diagnosis of ventricular tachycardia "can usually be made with confidence". The oesophageal lead is of great value in the electrocardiographic diagnosis of these conditions, and is essential in the differentiation of supraventricular tachycardia with bundle-branch block, ventricular tachycardia with independent auricular activity, ventricular

tachycardia with retrograde conduction, and ventricular tachycardia with auricular fibrillation.

[This is a stimulating, carefully coordinated paper which is deserving of careful study by all clinical cardiologists.] *William A. R. Thomson*

421. The Pulmonary Vein Wedge Pressure in Man
D. C. CONNOLLY and E. H. WOOD. *Circulation Research* [*Circulat. Res.*] 3, 7–13, Jan., 1955. 2 figs., 14 refs.

During the study by cardiac catheterization of patients with atrial septal defects or other congenital cardiac anomalies at the Mayo Clinic it was found possible to wedge a catheter into a branch of the pulmonary vein. In all cases the pressure recorded through this catheter (the "pulmonary vein wedge pressure") was higher than that in the unobstructed pulmonary vein and lower than that in the pulmonary artery, the latter difference increasing with the pulmonary arterial pressure. The oxygen saturation of blood from the catheter wedged in the pulmonary vein exceeded that of left atrial blood: this might be accounted for by a greater admixture of bronchial venous blood with pulmonary venous blood in the latter.

Measurement of the pulmonary "capillary" pressure by the usual technique of wedging a catheter into a branch of the pulmonary artery may give correct figures in normal subjects and where the pulmonary arterial resistance is very high, as in mitral stenosis. In intermediate circumstances, however, this method is unreliable. *J. McMichael*

CONGENITAL HEART DISEASE

422. Continuous Murmurs without Patent Ductus Arteriosus
R. E. BONHAM CARTER and C. H. M. WALKER. *Lancet* [*Lancet*] 1, 272–276, Feb. 5, 1955. 6 figs., 7 refs.

At the Hospital for Sick Children, Great Ormond Street, London, 5 children aged 3 months to 8 years were admitted with a continuous cardiac murmur in the pulmonary area, but none of the usual causes of this sign, including patent ductus arteriosus, could be found. Thoracotomy was carried out on 4 of the patients and of these 2 died, while a fifth child died soon after admission; in these 3 cases the absence of a patent ductus was confirmed at necropsy.

Apart from patent ductus arteriosus, a continuous murmur may be heard in cases of pulmonary atresia or persistent truncus arteriosus, where the lungs are supplied by the bronchial arteries. Other conditions, such as arterio-venous aneurysm of the lung, perforation of the sinus of Valsalva into the pulmonary artery or right ventricle, a continuous hum of venous origin, and congenital aorto-pulmonary defects may also have to be considered in the differential diagnosis of such cases. In all the five cases here reported multiple abnormalities were present as well, but a ventricular septal defect was common to 4 of them. In the fifth case the murmur was thought to be due to a large internal mammary artery associated with coarctation of the aorta. The use of phonocardiography in the diagnosis of such cases is discussed. The authors suggest that complicated ventricular septal defects and large tortuous collateral vessels should be added to the recognized causes of a continuous precordial murmur. *Keith Ball*

423. Venous Pulse in Atrial Septal Defect: a Clinical Sign
J. REINHOLD. *British Medical Journal* [*Brit. med. J.*] 1, 695–698, March 19, 1955. 3 figs., 10 refs.

Little attention has been paid to the value of the venous pulse wave in the neck as a physical sign of atrial septal defect. At the Hospital for Sick Children, Great Ormond Street, and St. Mary's Hospital, London, a study of the jugular phlebograms in 25 cases of atrial septal defect showed that the height of the *v* wave was the important feature, and this was therefore measured in relation to the height of the *a* wave. In normal subjects it was found that the *v* wave was slightly greater, equal to, or smaller than the *a* wave. In 13 out of 20 patients with uncomplicated atrial septal defect the *v* wave was "large" (2 to 3 times the height of the *a* wave) while in 7 it was "giant" (more than 3 times as high). In the remaining 5 cases in the series pulmonary hypertension was present and the *a* wave was large, making comparison with the *v* wave unprofitable; nevertheless, the latter was usually larger than normal.

It is pointed out that the characteristic pattern of the venous pulse in atrial septal defect consists of a deep systolic collapse (*x*) after the *c* wave, which is thought to be due to an exaggerated descent of the atrioventricular septum, followed by a sharply rising *v* wave and a well-marked diastolic collapse. The sharp rise in the *v* wave is probably due to rebound of the septum into the cavity of the auricle after systolic ejection, accompanied by overfilling of the right auricle by blood from the left auricle through the septal defect. Proper examination of the veins in the neck will demonstrate the exaggerated *v* wave, which immediately follows the second heart sound. *A. Paton*

CHRONIC VALVULAR DISEASE

424. The Clinical Estimation of Pulmonary Hypertension Accompanying Mitral Stenosis
N. O. FOWLER, W. J. NOBLE, S. J. GIARRATANO, and E. P. MANNIX. *American Heart Journal* [*Amer. Heart J.*] 49, 237–249, Feb., 1955. 5 figs., 6 refs.

An attempt was made to correlate the clinical findings with the pulmonary arterial blood pressure as measured by cardiac venous catheterization in 40 patients with mitral stenosis studied at Brooklyn Hospital (State University of New York), New York. The patients were divided into three groups: (1) pulmonary hypertension mild or absent (pressure below 30 mm. Hg), 18 cases; (2) moderate pulmonary hypertension (pressure 30 to 49 mm. Hg), 10 cases; and (3) severe pulmonary hypertension (pressure above 50 mm. Hg), 12 cases. No consistent correlation was found between the clinical findings and the degree of pulmonary hyper-

tension; the intensity of the apical diastolic murmur and of the pulmonary second sound were of no help, nor was the height of the " A " wave of the right atrial pressure pulse. Haemoptysis was more frequent in Group 3, but was encountered at all pressure levels. Pulmonary oedema did not occur in any case in which the pulmonary arterial pressure was below 22 mm. Hg, and was often absent at higher pressure levels. On the other hand if the transverse diameter of the heart was not greatly increased, radiological evidence of right ventricular hypertrophy usually indicated rather severe pulmonary hypertension.

The electrocardiographic findings occasionally gave some indication of the degree of pulmonary hypertension present, particularly precordial Lead V_1. Although there were exceptions, electrocardiographic evidence of right ventricular hypertrophy was generally absent when the mean pulmonary arterial pressure was below 28 mm. Hg, and present when the mean pulmonary arterial pressure was 42 mm. Hg or above.

William A. R. Thomson

425. **Does Mitral Stenosis Recur after Commissurotomy?**

R. P. GLOVER, J. C. DAVILA, T. J. E. O'NEILL, and O. H. JANTON. *Circulation* [*Circulation (N.Y.)*] **11**, 14–28, Jan., 1955. 8 figs., 18 refs.

An adequate commissurotomy, in the authors' view, is achieved by: (1) splitting the lateral commissure to the atrioventricular annulus to produce an orifice which will admit 2 fingers (3 to 4 cm.); (2) splitting the medial commissure only in those cases where lateral splitting does not produce an adequate orifice; (3) separating fused chordae tendineae to increase mobility of the cusps; and (4) ensuring that the lateral base of the valve is not displaced and pressed against the myocardium, giving a false impression of complete separation to the annulus.

In a series of 600 cases in which mitral commissurotomy was performed there were 42 deaths in the late postoperative period. Adequate records were available up to the time of death for 37 of these, in none of which could death be attributed to a recurrence of mitral stenosis. Necropsy reports in 31 cases showed that 20 patients died within 24 days of operation and 11 died between one and 18 months afterwards. In neither group was there any evidence of a recurrence of stenosis.

The authors then describe in detail 10 cases in which commissurotomy was performed in 1949. Three of the patients died in the immediate postoperative period; of the remaining 7, who had been under observation for 4½ to 5½ years, 5 were in good health without clinical evidence of recurrence. In one case there was no improvement, and the patient's condition was deteriorating, while in one tricuspid valvotomy was recently performed and an adequate assessment of the outcome was therefore not possible.

The authors conclude from their series of 600 cases that there is no good evidence to suggest that stenosis recurs during the first 5 years after commissurotomy " provided the operation has been properly performed ".

W. P. Cleland

426. **Long-term Results of Commissurotomy for Mitral Stenosis.** (Risultati a distanza negli operati di commissurotomia per stenosi mitralica)

A. COLLICELLI and L. LAI. *Cuore e circolazione* [*Cuore e Circol.*] **38**, 331–343, Dec., 1954. 3 figs., bibliography.

In a series of 126 mitral commissurotomies performed from November, 1950, to December, 1953, there were 17 deaths (12 during or immediately after the operation and 5 within 3 to 6 months) and 109 survivals. Eighty-two of the survivors have been followed up over periods of 1 to 3 years. Forty-three do not complain of any symptoms and their tolerance for even moderately severe effort is excellent; 35 have been greatly improved and only complain of mild dyspnea on exertion; and 4 showed no change.

No definite correlation appears to exist between the improvement of functional capacity and the modifications in the auscultatory signs of stenosis. On the other hand, the postoperative appearance of a systolic murmur apparently points to a less favourable evolution. There is a fairly good correlation between the regression of the electrocardiographic and the roentgenologic abnormalities and the clinical improvement.—[Authors' summary.]

HEART FAILURE

427. **Oral Administration of a Potent Carbonic Anhydrase Inhibitor (" Diamox "). III. Its Use as a Diuretic in Patients with Severe Congestive Heart Failure Due to Cor Pulmonale**

W. B. SCHWARTZ, A. S. RELMAN, and A. LEAF. *Annals of Internal Medicine* [*Ann. intern. Med.*] **42**, 79–89, Jan., 1955. 1 fig., 11 refs.

To 15 patients in various Boston hospitals with emphysema and 2 with kyphoscoliosis, all suffering from severe congestive heart failure due to chronic cor pulmonale, " diamox ", a carbonic anhydrase inhibitor, was administered on 18 occasions in doses ranging from 500 mg. once a day to 500 mg. every 6 hours. A profuse diuresis and consequent clinical improvement occurred in about one-half of the cases, the average weight loss being 15½ lb. (6·8 kg.) during 5 to 12 days of treatment. In the remaining cases no significant effect was seen.

It is suggested that the initial blood bicarbonate level, which was higher in those responding to diamox, was the only factor present which might have been responsible for the difference in response between these two groups. The good diuretic response in some of these patients contrasts with the absence of response in a previously reported series of patients with severe congestive failure but without respiratory acidosis (*New Engl. J. Med.*, 1954, **250**, 759 and 800; *Abstracts of World Medicine*, 1954, **16**, 446). It is pointed out that patients with cor pulmonale have an increased rate of renal tubular absorption of bicarbonate, and that in such circumstances inhibition of carbonic anhydrase would result in a large loss of sodium bicarbonate. Other aspects of the mode of action of diamox are discussed in the light of current theory.

A. Schott

428. Cerebral Vasothrombosis in Cardiac Diseases: Clinicopathologic Study

I. M. SCHEINKER. *Annals of Internal Medicine* [*Ann. intern. Med.*] **42**, 128–135, Jan., 1955. 4 figs., 7 refs.

The author calls attention to the frequent occurrence in cases of chronic heart failure of thrombotic occlusion of small cerebral veins in the absence of occlusion of large cerebral blood vessels, and in this paper from Flower and Fifth Avenue Hospitals, New York, describes 15 cases of chronic heart failure in which thrombosis of small cerebral veins resulting in haemorrhagic infarcts was found post mortem. Microscopically, only the earlier stages of thrombosis were found. The clinical manifestations during life consisted mainly in mental disturbances of various degrees and focal neurological signs, with in 2 cases focal or generalized epileptic seizures.

A. Schott

429. The Management of Refractory Edema in Heart Failure

A. L. RUBIN, H. G. THOMPSON, W. S. BRAVEMAN, and E. H. LUCKEY. *Annals of Internal Medicine* [*Ann. intern. Med.*] **42**, 358–368, Feb., 1955. 3 figs., 5 refs.

The management of refractory oedema due to cardiac failure is discussed, with special reference to 6 such cases treated at Cornell–Bellevue Hospital Center, New York. Most patients in heart failure ultimately develop refractory oedema, for which, in some cases, accompanying hyperthyroidism, infection, or hepatic and renal disease may be responsible. Commonly, however, continuous medication with mercurial diuretics leads to depletion of the plasma chloride content, with a corresponding elevation in bicarbonate level, and the patient responds less and less to mercurials. Responsiveness may be restored by administration of adequate doses of ammonium chloride but the necessary amounts may not be well tolerated.

Acetazoleamide (" diamox ") inhibits carbonic anhydrase in the renal tubules, thus promoting the excretion of an alkaline urine which carries with it increased amounts of sodium and potassium. As a result of this loss of base a hyperchloraemic acidosis develops in the plasma. In the authors' experience diamox alone may be ineffective as a diuretic, but after its administration restoration of responsiveness to mercurials has been observed. When the hyperchloraemia due to diamox is enhanced by administration of ammonium chloride an excellent response to mercurials is achieved. In the cases discussed administration of diamox and ammonium chloride for 3 to 6 days was followed by a good diuretic response to mercurials, which was usually best at 48 hours after the last dose of diamox. Close laboratory control is desirable, but in routine clinical use no untoward effects were noted in 20 patients.

[The dosage of diamox used is not mentioned; a commonly used dose is 250 mg. once daily.]

J. McMichael

430. Pulmonary Oedema

G. W. HAYWARD. *British Medical Journal* [*Brit. med. J.*] **1**, 1361–1367, June 4, 1955. 3 figs., 32 refs.

431. Prevention and Treatment of Hypertensive Heart-failure by Ganglion-blocking Agents

K. SHIRLEY SMITH and P. B. S. FOWLER. *Lancet* [*Lancet*] **1**, 417–418, Feb. 26, 1955. 7 refs.

The incidence and control of heart failure in 114 patients undergoing treatment with hexamethonium bromide or other ganglion-blocking agents for hypertension were studied at Charing Cross Hospital, London; 26 of the patients were in heart failure before treatment started. Congestive heart failure was present in 6 patients; to 3 of them digitalis and mersalyl were given initially, and after congestion had disappeared hexamethonium prevented a recurrence of failure; 3 received hexamethonium initially without success, digitalis and mersalyl being required eventually. In 14 patients with established left ventricular failure there was marked improvement with hexamethonium even though blood-pressure control was not maintained in several cases. Five of these patients have since died, 3 from cerebral vascular accidents and 2 from uraemia. In 6 patients early symptoms of left ventricular failure were completely relieved by hexamethonium. In none of the cases in the series did left ventricular failure develop for the first time during treatment. Of the 14 deaths, 6 were due to cerebral vascular accident, 5 to uraemia, and 2 to myocardial infarction; in 1 case the cause of death was not known. The authors do not consider that hexamethonium treatment is followed by an undue incidence of cerebral vascular accidents or of myocardial infarction, especially if a " retard " preparation is used.

K. G. Lowe

432. The Liver in Congestive Heart Failure

T. J. WHITE, C. M. LEEVY, A. M. BRUSCA, and A. M. GNASSI. *American Heart Journal* [*Amer. Heart J.*] **49**, 250–257, Feb., 1955. 1 fig., 34 refs.

A study of the clinical, biochemical, and histological findings in 75 adult patients with congestive heart failure is presented from Jersey City Medical Center. Hepatomegaly was present in 71 cases, ascites in 37, jaundice in 16, and liver pain in 9.

Liver function tests showed some biochemical abnormality to be present in every case: changes in serum protein levels were present in 100%, decreased glycogen storage in 93%, prothrombin deficiency in 90%, abnormal " bromsulphalein " retention in 78%, hyperglobulinaemia in 34%, and a positive thymol turbidity reaction in 11%.

Needle biopsy of the liver revealed a normal appearance or passive congestion in 63%, central necrosis with congestion in 9%, centrilobular fibrosis with congestion in 12%, diffuse fibrosis in 12%, fatty metamorphosis in 2·7%, and focal inflammation in 1·3%. It is recorded that the severity of the heart failure and the previous dietary habits were " important determinants of anatomic changes ". Severe heart failure was accompanied by central necrosis and exudation in the spaces of Disse. In one case followed up for 4 years recurrent episodes of failure led to centrilobular fibrosis.

There was close correlation between clinical and histological findings. Thus ascites was most prominent in

patients with centrilobular or diffuse fibrosis, while of the 16 cases in which jaundice was present it could be ascribed to hepatocellular changes alone in 11 (69%) and to a combination of liver-cell dysfunction and pulmonary infarction in 5 (31%). On the other hand there was no correlation between biochemical and histological findings. *William A. R. Thomson*

CORONARY DISEASE AND MYOCARDIAL INFARCTION

433. The Surgical Treatment of Myocardial Ischemia by Cardiopericardiopexy. [In English]
S. A. THOMPSON, L. A. AKOPIANTZ, and D. MOELLMANN. *Arquivos brasileiros de cardiologia* [*Arch. brasil. Cardiol.*] 7, 251–272, Dec., 1954. 3 figs., 46 refs.

Cardiopericardiopexy, an operation designed to increase the blood supply to the myocardium, is based on the following physiological principles. Magnesium silicate powder, when introduced into the pericardial sac of animals, produces a foreign-body reaction leading to a granulomatous pericarditis. Numerous mediastinal vessels enlarge to supply this granuloma, and gradually the blood supply of the myocardium is itself improved. The inflammatory reaction lasts for many years because the powder, owing to the large size of the particles, is not absorbed. No constrictive effects are observed.

Cardiopericardiopexy has been performed during a 14-year period in 57 cases of myocardial ischaemia. The 5th left costal cartilage was excised, the anterior mediastinum entered, and 2 to 4 g. of magnesium silicate powder was introduced into the pericardial sac, which was then loosely closed. The average age of the patients was 51 years and the average duration of symptoms 3½ years. In 37 cases the first symptom was angina and in 13 it was coronary occlusion. A recent unhealed infarction was considered to be a contra-indication to operation. Of the 57 patients, 7 died in hospital; of the remaining 50, who were followed up for 1 to 14 years, 45 were more than 50% improved, 20 being more than 75% improved. The average duration of life after onset of the first symptom was 9½ years, compared with 4½ years in a comparable series of patients not treated by operation. *R. L. Hurt*

434. Pericardial and Myocardial Vascularization following Cardiopericardiopexy. Magnesium Silicate Technique
A. PLACHTA, S. A. THOMPSON, and F. D. SPEER. *Archives of Pathology* [*Arch. Path. (Chicago)*] 59, 151–161, Feb., 1955. 15 figs., 34 refs.

Between November, 1938, and July, 1951, 57 patients with incapacitating coronary arterial disease were treated at the Flower and Fifth Avenue Hospitals (New York Medical College), New York, by pericardiotomy and the insertion of 4 to 6 g. of powdered magnesium silicate (talc powder, *U.S.P.*) into the pericardial sac. There were 7 postoperative deaths. Subsequent clinical improvement was noted in 45 of the survivors, of whom 17 have since died, having lived an average of 5 years after operation. The present report describes the findings in the heart at necropsy on 10 patients who died at intervals ranging from 1 day to 10 years after operation. [For further clinical details see Abstract 433 above.]

In all 10 cases talc particles were identifiable in the pericardium on histological examination by polarized light. An active aseptic inflammatory process had evidently continued in all since operation, causing obliteration of the pericardial space and the development of vascular adhesions between the heart surface and surrounding structures. There was no evidence of constrictive pericarditis. The adhesions contained arteries up to 1 mm. in internal diameter originating from the superior phrenic, internal mammary, bronchial, intercostal, and pulmonary arteries and from pericardial and oesophageal branches of the thoracic aorta. In 4 cases stained radio-opaque material was injected to enable these vessels to be traced by radiography and the examination of serial sections; they were shown to communicate with branches of the right and left coronary arteries. Fluid dye injected into the extra-cardiac sources of these vessels was seen to issue into the coronary sinus.

The authors suggest that the anastomoses produced by this operation remain patent because of the continued inflammatory reaction to the irritation set up by the talc. [No evidence is presented, however, to show that the direction of blood flow during life is into the coronary system.] *J. A. Cosh*

435. Ischaemic Heart Disease: a Statistical Study
D. STUCKEY. *Medical Journal of Australia* [*Med. J. Aust.*] 1, 169–171, Feb. 5, 1955. 1 fig., 14 refs.

The case histories of 9,000 patients referred to the National Heart Hospital, London, were reviewed and those of 1,600 (1,261 males and 339 females) with a diagnosis of ischaemic heart disease discriminated for study. Any patients with complicating conditions other than hypertension were excluded.

The relative age incidence of ischaemic heart disease in each sex was calculated by relating the data in this series to the population at risk in each age group as given by the 1951 census figures for England and Wales. From these relative rates it appears that the disease first appears at ages 25–29 in men and at 30–34 in women, its incidence rising to a peak in both at ages 60–64, and declining in the older age groups—this decline, in the author's view, being artificial and due to inadequacies in the data.

Taking a blood pressure of 160/100 mm. Hg as the upper limit of normal, the author found that 31% of the males and 56% of the females were hypertensive, proportions which are lower than those given in most previous reports. [The only series cited by the author which is strictly comparable in size, sex distribution, and criteria of hypertension is that of Cassidy (*Lancet*, 1946, 2, 587), who is quoted as having found that 55·4% of his male patients and 69·7% of his female patients had hypertension. However, reference to the original paper shows that this was not a sex distinction, the former figure being the incidence of hypertension in the whole series and the latter the incidence after "excluding those cases in which an existing or recent

coronary occlusion was thought to be responsible for a low blood pressure ".]

The over-all sex ratio (male to female) for ischaemic heart disease in this series was 3·7 to 1, varying from 7·5 to 1 at ages below 50 to only 2·6 to 1 at ages 65 and over, male preponderance being less pronounced amongst those with hypertension.

[Clarification or discussion of the following points would have enhanced the value of this paper. (1) Possible administrative factors affecting age and sex distribution. (2) Was the age distribution based on age at onset or age on admission? (3) Is the population served by the National Heart Hospital representative of that of England and Wales as a whole? (4) Is it justifiable to adopt the same criterion of hypertension for both sexes?]

E. Lewis-Faning

436. **The Role of Hypertension in the Etiology and Prognosis of Coronary Occlusion**

L. H. SIGLER. *Annals of Internal Medicine* [*Ann. intern. Med.*] **42**, 369–377, Feb., 1955. 26 refs.

The incidence of hypertension among patients with coronary arterial occlusion has been variously reported to range from 28 to 76%. Further to a previous study (*J. Amer. med. Ass.*, 1951, **146**, 998; *Abstracts of World Medicine*, 1951, **10**, 510) the author has now re-analysed the records of 1,160 patients with coronary occlusion, the highest blood pressure recorded in the interval being taken for purposes of classification. The following conclusions were drawn. Coronary occlusion reaches its fastigium between the ages of 50 and 59 in males and of 60 and 69 in females. It was found that 78% of males and 42% of females had a normal blood pressure at the time of the occlusion. A rising incidence of hypertension in males after the age of 60 is not accompanied by any parallel increase in the incidence of coronary occlusion. Coronary occlusion is 4·4 times as common in males as in females, while hypertension is twice as common in females as in males. It is concluded that the association of hypertension and coronary occlusion may thus be quite accidental. *J. McMichael*

437. **Four Years' Clinical Experience with Internal Mammary Artery Implantation in the Treatment of Human Coronary Artery Insufficiency Including Additional Experimental Studies**

A. VINEBERG, D. D. MUNRO, H. COHEN, and W. BULLER. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **29**, 1–36, Jan., 1955. 12 figs., 29 refs.

The 5-year survival rate of patients with angina pectoris is estimated from reports in the literature at 58%, while less than 50% of patients survive 5 years after their first attack of coronary occlusion. Moreover, few patients who have suffered infarction of heart muscle return to a full and active life. These figures indicate the danger of myocardial ischaemia and the potential value of any practicable method of providing a new blood supply to the threatened or damaged area. Successful revascularization by any such method can be shown only by the anatomical demonstration of new channels and by the ability of the myocardium to withstand further coronary insufficiency, and the present authors used these standards in assessing the results of implantation of the internal mammary artery into the myocardium in experimental animals. A variety of experiments were carried out to prove that an anastomosis is formed between the implanted vessel and the coronary system and to test the efficacy of the newly formed anastomosis. It was found that the formation of new channels seems " to be related to the heart's demand for fresh arterial blood " and that an implanted artery will branch and form new vessels most readily where the pressure differential between the graft and the heart is highest—as in an ischaemic area.

The selection of patients suitable for the implantation operation is discussed in detail and the technique is described. Of 28 patients treated by this method at the Royal Victoria Hospital, Montreal, 24 survived the operation, of whom 17 (70%) have been sufficiently improved to return to work. The follow-up period ranged from 2 months to 4 years. *T. Holmes Sellors*

438. **Arterialization of the Coronary Sinus in Occlusive Coronary Artery Disease. III. Coronary Flow in Dogs with Aorticocoronary Sinus Anastomosis of Six Months' Duration**

A. A. BAKST, A. ADAM, H. GOLDBERG, and C. P. BAILEY. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **29**, 188–196, Feb., 1955. 4 figs., 9 refs.

It has been established by Beck *et al.* (*J. Amer. med. Ass.*, 1951, **147**, 1726; *Abstracts of World Medicine*, 1952, **12**, 45) and confirmed by the present authors that arterialization of the coronary sinus in dogs by means of a free vein graft from the aorta provides a considerable degree of protection against the effects of ligation of the left circumflex coronary artery 4 to 8 weeks later. Further investigations are now reported from the Hahnemann Medical College and Hospital, Philadelphia, which were carried out with the object of determining whether or not this benefit persists for a longer period. The methods used are described in detail, and the findings in a series of dogs 6 months after arterialization of the coronary sinus are reported.

The volume of retrograde blood flow from the distal cut end of the ligated and transected circumflex coronary artery was five times greater than the expected normal, though it was less than it had been in the animals investigated 4 to 8 weeks after the anastomosis. The oxygen content of the blood approximated to that of aortic blood. Occlusion of the graft did not alter these findings, and it is therefore suggested that it is dispensable at this stage. Retroperfusion of the myocardial capillary bed, which was demonstrable 4 to 8 weeks after the operation, could no longer be demonstrated after 6 months, and the mortality from ligation of the retroflex coronary artery had risen from 20 to 66%. *J. R. Belcher*

439. ***In vivo* Microscopic Observations of the Circulating Blood in Acute Myocardial Infarction**

E. H. BLOCH. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **229**, 280–293, March, 1955. 40 refs.

AORTA

440. Aortic Arch Resection and Grafting for Aneurysm Employing an External Shunt

A. STRANAHAN, R. D. ALLEY, W. H. SEWELL, and H. W. KAUSEL. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **29**, 54–65, Jan., 1955. 7 figs., 19 refs.

Resection of the aortic arch in cases of aneurysm and its replacement by a graft is a formidable undertaking. From the Albany Hospital, New York, the authors here record 2 cases in which the thoracic aorta or a part of it was resected and replaced by a graft, the circulation being diverted during the manipulation through a large-calibre shunt made of "tygan" tubing with siliconed glass joints. In the first case the shunt ran from the ascending aorta to well below the aneurysm, a branch being inserted into the innominate artery. After removal of the greater part of the thoracic aorta and the left lung, which had to be sacrificed because of damage to the left pulmonary artery, continuity was restored by means of two lengths of freeze-dried calf's aorta joined together, the innominate and left carotid arteries being implanted into the side of the graft. The exposure involved opening both pleural cavities and 5 litres of blood were lost and replaced. The operation took 15 hours, during nearly 7 of which the aorta was excluded and the circulation maintained by the shunt. The patient died shortly after completion of the operation from haemorrhage from the left pulmonary artery, which had been cut through by the ligature applied on removal of the lung.

In the second case a traumatic aneurysm of the descending aorta was successfully resected and replaced by an 8-cm. homologous aortic graft. A shunt was arranged between the left subclavian artery and the descending aorta, the main trunk of the aorta being occluded for over 3 hours. The patient was discharged from hospital 27 days later.

From observations made during these two operations it is concluded that a shunt with an internal diameter of at least 1 cm. should be used if damage to the kidneys and spinal cord are to be avoided when the aorta is clamped off for any length of time. *T. Holmes Sellors*

441. Resection of the Thoracic Aorta with Replacement by Homograft for Aneurysms and Constrictive Lesions

D. A. COOLEY and M. E. DEBAKEY. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **29**, 66–104, Jan., 1955. 27 figs., 44 refs.

In this important article the authors discuss the problems involved in surgical excision of a portion of the thoracic aorta and restoration of continuity by means of a homograft in the treatment of constrictive lesions and aneurysms.

The basic limiting factor in surgery of the aorta is the length of time the aorta can be clamped during the reconstruction. The level of the occlusion is significant, and the spinal cord appears to be the structure most easily damaged by ischaemia; renal ischaemia is not so important. Obstruction of the aorta just below the arch may produce paraplegia, but clamping below the renal arteries is not likely to cause damage. The dangers of ischaemia are reduced by the presence of a collateral circulation, as in coarctation and long-standing aneurysms, but some of the collateral vessels may have to be severed during the operation. A number of technical points designed to minimize the risks merit consideration. Free and adequate exposure with full and free dissection of the part of the aorta to be excised are necessary preliminaries, and the graft should be prepared and the clamps applied beforehand. The time taken for restoration of continuity is usually 30 to 60 minutes. The use of a shunt during the occlusion period and of local or general hypothermia are other methods by which the risks of ischaemia can be reduced.

The 21 cases in which the authors have performed this operation at the Jefferson Davis and Methodist Hospitals (Baylor University College of Medicine), Houston, Texas, are described in some detail. The resection in 12 cases was undertaken for aneurysm and in 9 for a constrictive lesion. There were 3 deaths. General hypothermia was used in 4 cases and local hypothermia of the spine in another. The grafts used were freeze-dried or lyophilized preparations. *T. Holmes Sellors*

SYSTEMIC CIRCULATORY DISORDERS

442. Cardiovascular Actions of Sodium Nitroprusside in Animals and Hypertensive Patients

I. H. PAGE, A. C. CORCORAN, H. P. DUSTAN, and T. KOPPANYI. *Circulation* [*Circulation (N.Y.)*] **11**, 188–198, Feb., 1955. 2 figs., 10 refs.

In experiments carried out at the Cleveland Clinic Foundation, Cleveland, Ohio, sodium nitroprusside given intravenously to dogs produced a marked but transient fall in blood pressure, which could be repeated if the drug was given at intervals of about 10 minutes. It was shown that by controlled intravenous infusion of the drug it was possible to maintain the blood pressure at any desired level by altering the rate of flow. The drug seems to act directly on the vascular musculature and produces renal arterial and general vasodilatation. Intravenous infusion of the drug at a rate of about 100 μg. per minute proved very effective for the prolonged control of hypertensive encephalopathy.

When given by mouth to animals or to man the hypotensive effect of sodium nitroprusside was much less striking. The authors suggest that this is due to the fact that sodium nitroprusside given orally is broken down with the liberation of cyanogen, which is in turn converted into thiocyanate, it being this substance which is probably responsible for such hypotensive effect as follows oral administration. Indeed, both the therapeutic and toxic effects of sodium nitroprusside on oral administration to patients with hypertension were indistinguishable from those of thiocyanate.

C. Bruce Perry

443. The Effect of Thoracolumbar Sympathectomy on Headache in Essential Hypertension

F. G. ELLIS. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **104**, 51–54, 1955. 1 fig., 3 refs.

444. Severe Hypertension Treated with Hexamethonium Bromide in Retard Medium

H. J. Goldsmith, D. W. Beaven, and H. P. Lambert. *Lancet* [*Lancet*] **1**, 371–374, Feb. 19, 1955. 8 refs.

A long-acting preparation of hexamethonium bromide was used in the treatment at Central Middlesex Hospital, London, of 11 patients suffering from malignant hypertension and 15 from benign hypertension. The preparation consisted of a 20% solution of hexamethonium bromide in polyvidone with ephedrine to give a final concentration of 1 in 1,500. The patients were admitted to hospital for the first 3 to 5 weeks of treatment, and the drug was given by subcutaneous injection 8-hourly, beginning with a test dose of 20 mg. The final dosage varied from 80 to 400 mg. (most often 200 mg.) 8-hourly. The patients were taught to give the injections themselves after they left hospital. The results of this treatment were good; 10 patients with benign hypertension and 7 with malignant hypertension were treated for more than 3 months and the relief of left ventricular failure in the former group and of papilloedema in the latter was striking. Side-effects were not on the whole troublesome—although there was one death from paralytic ileus; they were much less frequent than with the soluble preparation and there was no period of incapacity following the injection. *G. S. Crockett*

445. The Effects of Intravenous Hexamethonium on Venous Pressure of Normotensive and Hypertensive Patients with and without Congestive Heart Failure

R. R. Burch. *Circulation* [*Circulation* (*N.Y.*)] **11**, 271–279, Feb., 1955. 4 figs., 8 refs.

At the Charity Hospital, New Orleans, 38 patients were given hexamethonium intravenously until the venous pressure began to fall or until 25 mg. had been given. The arterial and venous pressures and pulse and respiration rates were then recorded at hourly intervals until the venous pressure had returned to normal. Note was also made of any effect of the drug upon respiratory and cardiac rhythm.

The patients were grouped in four categories and the findings were as follows. (1) In 10 patients with normal arterial pressure and without congestive failure there was usually no change in either pressure. (2) In 9 normotensive patients with congestive heart failure there was an average fall in venous pressure of 80 mm. H_2O, and in arterial pressure of 38 mm. Hg; both pressures returned to normal within 2 hours in 4 cases, but the effect was more prolonged in the others—in one the venous pressure remained low for more than 13 hours. (3) In 10 hypertensive patients without congestive failure the arterial pressure fell by an average of 47 mm. Hg and in half of the cases there was also a moderate fall in venous pressure, averaging 14 mm. H_2O. (4) In 9 patients with hypertension and congestive failure the venous pressure fell by an average of 88 mm. H_2O and the arterial pressure by 44 mm. Hg. In 4 cases the venous pressure returned to normal within 3 hours; in the others it remained low for longer—over 8 hours in one case. The average dose of hexamethonium given in Group 3 was 22·8 mg. and in Group 4 21 mg., but in Group 2 an average dose of only 10·1 mg. was needed to cause a fall in venous pressure. All dyspnoeic patients improved, especially those with pulmonary oedema. Gallop rhythm and pulsus alternans sometimes disappeared. These observations are interesting in that they show conclusively that there is an increase in venous tone in congestive failure. They also indicate that hexamethonium may have a place in the treatment of that condition. *C. W. C. Bain*

446. The Circulatory Effects of Reserpine

E. G. McQueen, A. E. Doyle, and F. H. Smirk. *Circulation* [*Circulation* (*N.Y.*)] **11**, 161–169, Feb., 1955. 7 figs., 12 refs.

At Otago University Medical School, Dunedin, New Zealand, reserpine, an alkaloid of *Rauwolfia serpentina*, was administered to 33 patients with hypertension and to 12 subjects with normal blood pressure in doses of 2 to 3 mg. three times a day by mouth. In the hypertensive patients the resulting reduction in blood pressure varied very widely; the maximum effect was noted within 48 hours and was associated with flushing, injection of the conjunctivae, and bradycardia, some patients also complaining of diarrhoea, shivering, tremor, mental depression, nightmares, insomnia, or extreme drowsiness. When smaller doses (0·5 to 1·5 mg. daily) were given such severe side-effects did not occur, but the maximum hypotensive effect was not seen for about 14 days. In the subjects with normal blood pressure the hypotensive effects of reserpine were much less marked.

In a series of experiments on rabbits reserpine produced cutaneous vasodilatation which was shown to be mediated, at least in part, by the sympathetic nervous system, since it was abolished by section of the cervical sympathetic trunk. However, in anaesthetized rabbits there was evidence of a direct vasodilator effect on blood vessels, and it is suggested that the drug may have a direct peripheral vasodilator effect in man. *C. Bruce Perry*

447. Treatment of Hypertension with Reserpine, with Reserpine in Combination with Pentapyrrolidinium, and with Reserpine in Combination with Veratrum Alkaloids

A. E. Doyle, E. G. McQueen, and F. H. Smirk. *Circulation* [*Circulation* (*N.Y.*)] **11**, 170–181, Feb., 1955. 21 refs.

At Otago University Medical School the authors found that reserpine in doses of 9 mg. daily lowered the blood pressure in most hypertensive patients, but the side-effects were so severe as to make treatment with these doses impracticable. When the alkaloid was given to 40 patients with hypertension in doses of 0·5 to 1·5 mg. daily serious side-effects were avoided and blood pressure was adequately controlled in 10.

In a further study 66 hypertensive patients were treated with a combination of reserpine and pentapyrrolidinium. In the majority of these cases the results were better than those obtained with pentapyrrolidinium alone, and also a smaller dose of the latter drug was required. However, a trial of reserpine in combination with veratrum viride in 10 cases was much less successful. The

authors suggest that some patients with mild hypertension may well be treated with reserpine alone, but that for those with severe hypertension the combination of reserpine and pentapyrrolidinium is the most satisfactory treatment at present available. *C. Bruce Perry*

448. **Combined Rauwolfia–Hydralazine Therapy of Hypertensive Patients**

C. F. NAEGELE, R. H. ROSENMAN, C. L. HOFFMAN, and M. FRIEDMAN. *Circulation* [*Circulation (N.Y.)*] **11**, 182–187, Feb., 1955. 11 refs.

At the U.S. Public Health Service and Mount Zion Hospitals, San Francisco, 9 in-patients with essential hypertension and 4 with "renal" hypertension were treated for one week with 4 mg. of "rauwiloid" (a preparation of the alkaloids of *Rauwolfia serpentina*) daily together with hydrallazine in doses varying from 75 to 300 mg. daily. At the same time 33 out-patients (26 with essential and 7 with renal hypertension) were treated similarly. Most of the patients in both series with mild or moderate hypertension showed an adequate lowering of the blood pressure, but the response in those with severe chronic hypertension and in those with renal hypertension was less satisfactory. The authors believe that the initial treatment with *Rauwolfia* alkaloids enabled an adequate lowering of the blood pressure to be achieved with moderate doses of hydrallazine, thus avoiding the serious side-effects often caused by the latter. *C. Bruce Perry*

449. **Arteriographic Appearances of the Digital Arteries of the Hands in Raynaud's Disease**

R. B. LYNN, R. E. STEINER, and F. A. K. VAN WYK. *Lancet* [*Lancet*] **1**, 471–474, March 5, 1955. 7 figs., 6 refs.

It is first pointed out that Raynaud's original observations on intermittent spasm of the digital arteries associated with colour changes were made in a number of conditions, including scleroderma, thrombo-angiitis obliterans, and atherosclerosis, and that the "acceptance of all these as Raynaud's disease has been primarily responsible for the confusion which followed his work". The authors, at the Postgraduate Medical School of London, studied by arteriography the blood vessels of both hands of 23 patients (9 males and 14 females) who had intermittent spasm and colour changes in the fingers. Arteriographs were obtained after 15 ml. of 50% diodone had been introduced into the exposed brachial artery above the elbow, the patient having first been anaesthetized. Examination of the arteriograms revealed two distinct groups of patients: (1) those with anatomically normal digital arteries and (2) those with obliteration of the digital arteries. It was also found that these two groups could be distinguished clinically, since patients with nutritional changes in the fingers were those in whom arterial obliteration was demonstrable. The authors suggest the term "thrombotic digital-artery disease" to describe the condition in this latter group, the term Raynaud's phenomenon being confined to intermittent spasm of the digital arteries unaccompanied by anatomical or nutritional abnormalities. In the authors' view this distinction is important in treatment because patients with Raynaud's phenomenon respond to vasodilator agents, such as tolazoline, and to sympathectomy, whereas patients with thrombotic digital artery disease are not helped by sympathectomy.

The authors conclude that arteriography is a safe and satisfactory method of distinguishing between these two types of case. *Leon Gillis*

PORTAL HYPERTENSION

450. **The Surgical Treatment of Portal Hypertension.** [In English]

C. A. EKMAN and P. SANDBLOM. *Acta chirurgica Scandinavica* [*Acta chir. scand.*] **108**, 241–260, 1954. 3 figs., bibliography.

In this paper from the Lund Hospital, Sweden, the surgical treatment of 43 cases of portal hypertension is discussed. In 19 cases the obstruction of the portal vein was extrahepatic and in 24 it was intrahepatic. Gastro-intestinal haemorrhage was the presenting symptom in 40 cases. Ascites was present in 13 cases, in all of which there was intrahepatic obstruction with decreased liver function. Radiological examination, which is considered to be a reliable diagnostic procedure, revealed the presence of oesophageal varices in 42 cases. It was also employed to judge the efficacy of the shunt operation; in 6 cases in which the radiological appearances were unchanged haemorrhage recurred. The authors found splenography of considerable help in deciding the site of the obstruction.

The authors state that porta-caval anastomosis is invariably impracticable in cases of extrahepatic obstruction, and lieno-renal anastomosis must be attempted. This was performed on 9 of 11 patients with intact spleen; in 2 obliteration of the shunt took place and the patients died from recurrent haemorrhage. The authors emphasize the difficulty of treating patients who have undergone splenectomy; 8 such patients in this series were subjected to various procedures and 3 died from recurrent haemorrhage. Of the 19 patients in this group 17 were under 20 years of age.

Of the 24 patients with intrahepatic obstruction, 3 underwent splenectomy only, and all 3 died within 6 weeks of operation. Lieno-renal anastomosis was carried out on 7 patients, 5 of whom were well, one had a recurrence of haemorrhage, and one died later of liver failure. Porta-caval anastomosis was performed in 14 cases; there were 3 postoperative deaths, 4 patients died subsequently—one from liver failure and the others from unrelated disease—and 7 were free from symptoms.

The authors conclude that for extrahepatic portal obstruction lieno-renal anastomosis through a thoraco-abdominal incision is the treatment of choice; splenectomy is to be avoided. In patients with intrahepatic obstruction and good liver function porta-caval anastomosis through a similar incision should be performed. When liver function is poor or ascites is present operation is hazardous because liver failure rapidly supervenes. *A. G. Parks*

Haematology

451. **Rheumatoid Purpura Treated with ACTH, Cortisone, and " 4560 RP ". (A Series of Five Cases).** (Purpura rhumatoïde [ACTH, cortisone, 4560 RP] (à propos de 5 observations)
L. LANGERON, G. FRUCHART, A. DESTOMBES, and E. LEMAIRE. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **70**, 917–921, Oct. 22, 1954. 1 ref.

Rheumatoid purpura, or Schönlein–Henoch's disease, is characterized by a cutaneous purpuric eruption, abdominal and renal symptoms, and a generalized arthralgia and oedema. The authors present 5 cases in which the administration of ACTH or cortisone, and in some cases " 4560 RP ", resulted in marked improvement or cure. The authors regard the condition as a consequence of irritation of the sympathetic nervous system, and emphasize the value of skin biopsy in diagnosis. *Kate Maunsell*

452. **Observations on the Antibody Content of the Blood in Patients with Multiple Myeloma**
H. A. LAWSON, C. A. STUART, A. M. PAULL, A. M. PHILLIPS, and R. W. PHILLIPS. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 13–18, Jan. 6, 1955. 3 figs., 13 refs.

The authors have studied at the Veterans Administration Hospital, Providence, Rhode Island, the occurrence and titre of circulating antibodies in the blood of 9 patients with multiple myeloma. In 4 of these cases there was complete absence of antibodies, including blood-group antibodies, and of the other 5 cases, 4 showed deficiency or absence of the antibodies sought for, namely, agglutinins for *Salmonella typhosa*, *Paracolobactrum ballerup*, and *Escherichia* (*Bacterium*) *coli*. Amboceptor was not detectable in any of the patients, although it was present in 97% of a large control group. Where some antibodies were present repeated examination revealed a progressive decrease. In 5 cases, including the 4 patients with complete absence of antibodies, filter-paper electrophoresis showed a marked increase in the plasma gamma-globulin fraction. *Marjorie Le Vay*

453. **The Management of Acute Leukaemia in Adults**
F. G. J. HAYHOE and L. WHITBY. *British Journal of Haematology* [*Brit. J. Haemat.*] **1**, 1–19, Jan., 1955. 6 figs., 47 refs.

In this paper from the University of Cambridge 50 cases of acute leukaemia seen during the last 5 years are discussed. All the patients were over 14 years of age. In 14 out of 41 patients given transfusions of 4 to 20 pints (2·3 to 11·4 litres) of whole blood there was a significant degree of improvement, 5 experiencing remissions lasting 2 to 6 months. From their experience in the treatment of the cases in which transfusion was not effective the authors state that they prefer cortisone and ACTH (corticotrophin) in lymphocytic leukaemia and aleukaemic myelocytic leukaemia, and 6-mercaptopurine in monocytic leukaemia and in the myelocytic group with a frankly leukaemic blood picture. They conclude that when a patient becomes refractory to a steroid or to 6-mercaptopurine a change to the other agent or a combination of both may be effective.
P. C. Reynell

454. **Experiemental Studies of Dimethanosulphonoxybutane and its Use in the Treatment of Myeloid Leukaemia.** (Indagini sperimentali sul dimetanosulfonossibutano e suo impiego nella terapia della mielosi leucemica cronica)
D. GIGANTE, S. TEODORI, and A. ZOPPINI. *Minerva medica* [*Minerva med.* (*Torino*)] **1**, 221–227, Jan. 27, 1955. 12 figs., 13 refs.

After reviewing the relevant literature, the authors report their own experimental and clinical experience at the Institute of Clinical Medicine of the University of Rome in the treatment of chronic myeloid leukaemia with dimethanosulphonoxybutane. The toxic effect of the drug was investigated in experiments on male rabbits, which were given a single dose of 50, 75, or 150 mg. per kg. body weight by stomach tube, the blood and the bone marrow being examined daily thereafter until the animals either died or recovered. In all cases there was a reduction in the leucocyte count to about 50% of the initial value within 4 days. The animals given 50 mg. per kg. recovered, the leucocyte count becoming normal again after about 10 days, whereas in the two other series the leucopenia was progressive and the rabbits died. Although the granulocyte count had fallen by 50% 24 to 48 hours after administration of the drug, the lymphocyte count was at first unaffected and subsequently fell by only about 20 to 30%. With doses of 50 to 75 mg. there was little or no reduction in the erythrocyte and platelet counts, but after administration of 150 mg. per kg. both were markedly reduced. The bone marrow of the animals given the larger doses showed the typical picture of aplastic anaemia.

Dimethanosulphonoxybutane was then administered to 14 patients suffering from chronic myeloid leukaemia, 5 of whom had received no previous treatment. The drug was given by mouth in a daily dosage of 10 to 20 mg. spread over the 24 hours, 2 to 3 mg. being given at a time. Administration was stopped when the leucocyte count had fallen to 15,000 or 20,000 per c.mm. in order to avoid causing aplastic changes in the bone marrow. The treatment lasted 16 to 32 days (total dose 220 to 585 mg.), depending on the patient's clinical and haematological condition. Blood counts were performed daily, and examination of the bone marrow took place before and after treatment. All the patients responded to the treatment, a virtually complete haematological remission with marked reduction in size of the spleen being obtained in 7 cases and a less complete remission in the remainder. The clinical condition was similarly improved, with

return of appetite and strength, and no toxic manifestations were observed. No difference in response was found between those patients who had previously received other forms of treatment for their condition and those who had not.

The average duration of remission cannot yet be determined; the first patient treated remains in complete remission after 5 months, whereas in 2 other cases the leucocyte count started to rise again 10 and 50 days respectively after finishing treatment.

Franz Heimann

455. **Hodgkin's Disease: an Analysis of Frequency, Distribution and Mortality at the University of California Hospital, 1914–1951**

M. B. SHIMKIN, K. C. OPPERMANN, W. L. BOSTICK, and B. V. A. LOW-BEER. *Annals of Internal Medicine* [*Ann. intern. Med.*] **42**, 136–153, Jan., 1955. 2 figs., 26 refs.

This paper forms the fourth of a series of detailed statistical analyses of the frequency, distribution, and mortality from neoplastic diseases of the lymphatic and haematopoietic tissues in patients seen by the authors at the University of California Hospital, San Francisco, between 1914 and 1951. A total of 254 cases of Hodgkin's disease were analysed according to sex, age at time of onset, duration of illness, stage of the disease, mortality, and effects of treatment, and the results compared with those from other centres. During the 37 years of observation there has been a progressive change in the sex ratio, a rising proportion of females being affected. Though there has been no change in the duration of the illness, there has been a gradual shift towards a higher age at onset and at death. No significant correlation could be demonstrated between duration of the illness and any specific therapy. The use of nitrogen mustard has not resulted in any prolongation of life.

H. Payling Wright

456. **A Clinical Evaluation of Colchicine in the Treatment of Hodgkin's Disease**

A. GROLLMAN, R. L. JOHNSON, and W. W. REGAN. *Annals of Internal Medicine* [*Ann. intern. Med.*] **42**, 154–170, Jan., 1955. 6 figs., 9 refs.

There has recently been renewed interest in various derivatives of *Colchicum autumnale* L. as mitotic depressants in the treatment of neoplasia. Following a report by Isch-Wall (*Sang*, 1952, **23**, 689) of good results with these substances in 4 cases of Hodgkin's disease the authors, working at the University of Texas Southwestern Medical School, have treated 10 patients with advanced Hodgkin's disease with intravenous injections of colchicine in doses of 3 mg. in isotonic saline every third day. The results seem to offer further evidence of the value of this drug. Detailed histories of the 10 cases show that in every instance there was some amelioration of symptoms, although this improvement was frequently only transitory. It is thought that, if combined with irradiation therapy, it may prove of considerable value. The drug is antipyretic and induces euphoria; in the authors' opinion it can usefully be given when the patient has become refractory to other forms of treatment.

H. Payling Wright

457. **The Relationship between Intrinsic Factor and the Intestinal Absorption of Vitamin B_{12}**

S. J. BAKER and D. L. MOLLIN. *British Journal of Haematology* [*Brit. J. Haemat.*] **1**, 46–51, Jan., 1955. 5 figs., 12 refs.

The authors, working at the Postgraduate Medical School of London, have studied the effect of intrinsic factor (I.F.) on the intestinal uptake of vitamin B_{12} (cyanocobalamin) in patients with pernicious anaemia in remission following treatment with the vitamin (in whom the effect of naturally-secreted I.F. could be assumed to be minimal). At least 14 days after the last therapeutic dose had been given, vitamin B_{12} labelled with radioactive cobalt (^{58}Co) was given by mouth together with varying amounts of pooled gastric juice or a dried preparation of hog's stomach as a source of intrinsic factor and the amount of radioactivity appearing in the faeces measured, the difference between the amount given and the amount so excreted being taken to represent the amount absorbed.

It was shown that, over a certain range, the uptake of vitamin B_{12} is directly proportional to the amount of I.F. administered, although the slope of the "absorption gradient" varied widely in different subjects. Beyond a certain point no more vitamin B_{12} is absorbed no matter how much I.F. is given. In another experiment it was shown that if the dose of I.F. remains constant the amount of vitamin B_{12} absorbed also remains constant, whatever the dose given. On the other hand the absorption of vitamin B_{12} given by mouth may be inhibited by the intramuscular administration of very large doses of the vitamin.

E. G. Rees

458. **Effect of Ultraviolet Radiation on the Infectivity of Icterogenic Plasma**

R. MURRAY, J. W. OLIPHANT, J. T. TRIPP, B. HAMPIL, F. RATNER, W. C. L. DIEFENBACH, and H. GELLER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 8–14, Jan. 1, 1955. 4 figs., 18 refs.

Experiments were carried out at the National Institutes of Health, Bethesda, Maryland, to determine the effect of ultraviolet irradiation on the infectivity of icterogenic plasma. The contaminating material consisted of plasma from subjects who had been inoculated with the Fort Bragg strain of serum hepatitis virus and of 4 presumably infectious units of plasma or serum from patients in the acute stage of serum hepatitis. To 10 litres of normal pooled plasma 980 ml. of this presumably infected plasma and serum was added. The infected plasma or serum was tested at dilutions ranging from 10^{-3} to 10^{-8}, and 1 ml. was injected into each of a number of volunteer subjects.

The material was infectious up to a dilution of 10^{-4}, but because of the small number of volunteers, icterogenicity in higher dilutions could not be excluded. Irradiation of the infected pool was carried out by the Dill Irradiator, the Habel–Sockrider Irradiator, and the Oppenheimer–Levinson Centrifugal Filmer. There was failure to inactivate the serum by all three methods, unless irradiation was so intensive as to cause changes in the plasma proteins.

Kate Maunsell

Respiratory System

459. **Diagnostic Significance of Pulmonary Hypertrophic Osteoarthropathy**
A. VOGL, S. BLUMENFELD, and L. B. GUTNER. *American Journal of Medicine* [*Amer. J. Med.*] **18**, 51–65, Jan., 1955. 20 figs., bibliography.

From the Metropolitan Hospital, New York, 7 cases of pulmonary hypertrophic osteoarthropathy associated with pulmonary disease are reported, in 6 of which there was bronchial carcinoma and in one a lung abscess. The classic features of pulmonary hypertrophic osteoarthropathy were present in all cases—namely, bone pain, stiffness of the fingers, muscle weakness, broadened finger ends, and redness and warmth of the overlying skin, the bone tenderness improving after removal of the underlying cause. In 5 of the 7 cases the presenting symptoms were referable to the extremities, and in some the appearances strongly suggested rheumatoid arthritis. In one case the bone changes did not give rise to symptoms. The authors consider that pulmonary hypertrophic osteoarthropathy is the outcome of a sustained increase in arterial flow with capillary stasis, caused by some pathological intrathoracic reflex. They state that there is no reported case of pulmonary hypertrophic osteoarthropathy due to uncomplicated pulmonary tuberculosis, and therefore the presence of clubbing in a case of doubtful aetiology would favour a diagnosis of carcinoma rather than of pulmonary tuberculosis. A careful search for pulmonary hypertrophic osteoarthropathy, including radiological examination, should be carried out in any case of lung disease in which the diagnosis is in doubt. *A. Gordon Beckett*

460. **Acute, Transient Middle Lobe Disease**
E. ROSENMAN. *Diseases of the Chest* [*Dis. Chest*] **27**, 80–87, Jan., 1955. 4 figs., 11 refs.

After reviewing the literature on atelectasis of the middle lobe of the lung the author describes in detail 4 cases of acute transient atelectasis of the right middle lobe, with or without acute pneumonitis, in all of which the condition cleared up completely within 1 to 4 weeks. It is pointed out that the middle-lobe bronchus is narrow and easily compressed because of the acute angle it forms with the main bronchus. The positioning of the middle-lobe bronchus may hinder adequate drainage from the middle lobe, leading to greater frequency of recurrent atelectasis and pneumonitis in this lobe than in others. This is the case in adults particularly. In children lobar atelectasis occurs without any predilection for any one lobe. The author suggests that the term " middle-lobe syndrome " should be an all-inclusive one for cases of middle-lobe atelectasis, regardless of aetiology, and that the term " middle-lobe disease " be used for cases of atelectasis and pneumonitis which are not caused by active tuberculosis or by neoplasm. " While conceivably some cases [of middle-lobe disease] might have been caused originally by tuberculous lymphadenitis in childhood, the resultant pneumonitis later in life is non-specific."

The author emphasizes the importance of fluoroscopy in the lordotic position to facilitate diagnosis of this condition. *John Taubman*

461. **Bronchial Carcinoma—a Pandemic. II. Incidence and Tobacco Consumption in Various Countries**
A. NIELSEN and J. CLEMMENSEN. *Danish Medical Bulletin* [*Dan. med. Bull.*] **1**, 194–199, Dec., 1954. 20 figs., 18 refs.

The relationship between the crude mortality from cancer of the lung among men in 1950 (or thereabouts) in each of 7 European countries and Canada and the consumption of tobacco and cigarettes per person in 1930 and 1950 in those countries is studied. Little correlation can be shown to exist between cancer mortality and the total tobacco consumption, but a fairly close linear relationship exists between cancer mortality and the consumption of cigarettes 20 years previously, when, it is assumed, tobacco and cigarette consumption was determined " in the main " by the amounts consumed by males. That no clear relationship can be demonstrated between mortality from cancer of the lung and contemporary cigarette consumption may be attributable to changes in the proportion of women among cigarette smokers during the last 20 years.

Graphs are also presented to show the increase in mortality from cancer of the lung between (about) 1925 and 1952 for Denmark, Norway, Switzerland, Holland, Finland, England and Wales, and Canada, the figures for men and women in each case being shown separately. Other graphs show the mortality from cancer of the lung at various ages among males and females in the same countries and in Sweden in 1949–51 and the mortality at different ages for cohorts born in various years in Switzerland, Holland, and Canada. The patterns in each case are similar, though there are considerable differences in the extent to which the crude mortality has increased among men. *Richard Doll*

462. **Chronic Bronchitis. An Attempt to Control Chronic Infection with *Haemophilus influenzae* by Aerosol Therapy**
K. KNOX, P. C. ELMES, and C. M. FLETCHER. *Lancet* [*Lancet*] **1**, 120–122, Jan. 15, 1955. 8 refs.

In an attempt to control chronic infection with *Haemophilus influenzae* an aerosol containing 400,000 units of benzylpenicillin and 0·4 g. of streptomycin sulphate dissolved in 1·5 ml. of 0·5% isoprenaline sulphate was given twice daily to patients with chronic bronchitis at the Hammersmith Hospital, London. It was found that this method could not be relied upon to control bronchial infection with this organism. The infection was controlled for 6 months in only one out of 6 out-patients,

and immediately treatment ceased *H. influenzae* reappeared in the sputum. In the other 5 cases the organism persisted in the sputum, although it appeared to retain its original sensitivity to penicillin and streptomycin. The authors suggest that the uneven distribution of the aerosol in emphysematous patients prevented the entry of the antibiotics into parts of the lung in which the organisms persisted. *J. G. Scadding*

463. **Aerosol Therapy with the Enzyme Deoxyribonuclease in Chronic Bronchial Affections.** (Aerosolterapia con l'enzima desossiribonucleasi nelle affezioni bronchiali croniche)
G. BERTELLI. *Minerva medica* [*Minerva med. (Torino)*] 1, 415–418, Feb. 14, 1955. 2 figs., 20 refs.

At the Medical Clinic of the University of Sienna, 2 patients with bronchiectasis and 3 with chronic bronchitis and mucopurulent sputum were treated with 10 to 15 mg. of deoxyribonuclease in the form of an aerosol, 2 or 3 inhalations being given per day for 5 to 14 days. In all 5 cases the amount of sputum decreased rapidly, and it became less purulent or fetid.

[The method of aerosolization and droplet size are not mentioned, and the mode of action of the aerosol is difficult to understand. If the droplets were large, say, 3 μ in diameter or more, they would hardly penetrate into the medium and small bronchi; and even if some were smaller the total amount reaching the thick viscous layer of mucus on the surface of these bronchi would be negligible.] *H. Herxheimer*

464. **The Maximal Diffusing Capacity of the Lung in Chronic Obstructive Disease of the Airways**
R. H. SHEPARD, J. E. COHN, G. COHEN, B. W. ARMSTRONG, D. G. CARROLL, H. DONOSO, and R. L. RILEY. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] 71, 249–259, Feb., 1955. 12 refs.

If the diffusing capacity of the lungs is measured during increasing grades of exercise a certain value is eventually reached which cannot be exceeded, implying that this value is a function of the whole diffusing surface of the lung. At Johns Hopkins University and Hospital, Baltimore, the authors studied 27 patients who had mild or moderate chronic airway obstruction with a minimum of other respiratory disease. Total lung volume and maximum breathing capacity were measured, and expired gas and arterial blood were collected during exercise on a treadmill while the patients breathed gas mixtures containing two different oxygen concentrations; from these data venous admixture and diffusing capacity could then be calculated.

Diffusing capacity was found to be normal in only 6 of the subjects, being reduced in the remainder, which included all the patients with cardiac involvement. Comparison of these values with those for lung volume, ventilatory capacity, and rate of removal showed a poor correlation, suggesting that there need be no relation between the degree of airway obstruction and the degree of damage to the lung's diffusing surface. This, the authors suggest, may account for differences in the assessments of the clinician, who observes primarily the degree of airway obstruction, and the pathologist, who is interested in the extent of damage to the alveolar walls. In addition, a reduction in the maximum diffusing capacity may be produced by damage to the pulmonary capillaries or thickening of the pulmonary membrane. *D. Goldman*

465. **The Effects of Carbonic Anhydrase Inhibitor on Arterial Blood Gases in Chronic Pulmonary Emphysema: a Preliminary Report**
H. A. LYONS, M. N. ZUHDI, and D. M. KYDD. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] 229, 193–198, Feb., 1955. 18 refs.

At Kings County Hospital, Brooklyn, New York, carbonic anhydrase inhibitor (2-acetylamino-1:3:4-thiodiazole-5-sulphonamide; " diamox ") was given in doses of 250 mg. twice daily to 9 patients with emphysema. The arterial carbon dioxide tension (pCO_2) fell in 6, remained unchanged in 2, and actually rose in one.

Detailed studies showed that the pCO_2 was initially greater than 50 mm. Hg in 4 patients, of whom 3 showed a significant decrease accompanied by symptomatic improvement. It was between 40 and 50 mm. Hg in 3 others, all of whom showed a decrease in pCO_2, but only one improved subjectively and one felt worse. The drug appeared to produce no alteration in pulmonary ventilation or cardiac output. *J. R. Bignall*

466. **Action of Breathing Exercises in Pulmonary Emphysema**
E. J. M. CAMPBELL and J. FRIEND. *Lancet* [*Lancet*] 1, 325–329, Feb. 12, 1955. 4 figs., 11 refs.

Lung function tests and electromyography of respiratory muscles were carried out on 12 patients with emphysema before and after a course of instruction in breathing exercises. The patients, all males, had been seen repeatedly at the Middlesex Hospital, London, but no improvement in respiration had been noted.

When the patients " breathed as they had been taught " there were a decrease in the rate and an increase in the depth of breathing. This maintained a normal alveolar ventilation while reducing the total ventilatory volume per minute. However, this alveolar ventilation was no more effective than before, since the mixing efficiency and the proportion of poorly ventilated alveoli were unchanged. Expiration was prolonged, the chest was less inflated, and there was increased electromyographic activity of the expiratory abdominal muscles during performance of the exercises. However, when hyperventilation was attempted by rebreathing expired air the patient was then unable to breathe as he was taught, and electrical activity stopped in the expiratory abdominal muscles. The performance of breathing exercises over a 3-month follow-up period had no demonstrable effect on lung function, since maximum breathing capacity, residual volume, and mixing efficiency were unchanged. *W. A. Briscoe*

467. **Intrapleural Enzymatic Debridement with Tryptar**
H. H. SEILER. *Diseases of the Chest* [*Dis. Chest*] 27, 179–189, Feb., 1955. 14 figs., 3 refs.

Otorhinolaryngology

468 (*a*). **Mobilization of the Stapes for Otosclerotic Deafness**

S. ROSEN and M. BERGMAN. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **61**, 197–206, Feb., 1955. 19 figs., 21 refs.

468 (*b*). **Revision of the Miot Technique in Mobilization of the Ossicle System. Its Otoneurologic and Acoustic Basis**

D. E. SCHNEIDER. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **61**, 207–211, Feb., 1955. 8 refs.

Of these two papers, the first describes a modification of the technique of mobilization of the stapes introduced in 1890 by Miot, whereby the authors claim to have improved hearing in 14 cases of otosclerosis treated at Mount Sinai Hospital, New York. With the original technique Miot obtained " slight and only temporary " improvement in 200 cases, and it was subsequently abandoned. In the operation performed by the authors the tympanic membrane is reflected upwards and the footpiece of the stapes mobilized by pulling on its neck in the line of stapedius tendon with a special curved " mobilizer " until it gives way, " sometimes with an audible crack ". To determine the force which may be safely used, the breaking strain of the crura of the stapes was measured in 31 excised specimens, the mean value being 166 g. (standard deviation 58 g.).

The author of the second paper criticizes this work on several grounds. He reasserts his belief in a surviving " primitive sonic system " acting through the tympanic plexus, and claims that this plexus is the primary site of the process resulting in otosclerosis—a trophic disease of the oval window producing ankylosis of the stapes. He discounts the practical value of the modifications introduced by Rosen into Miot's technique, and claims that the results obtained by the former are not so good as those which the latter reported, and must be accepted with caution. Lastly, he complains that Rosen has misinterpreted his (the author's) theory of a dual hearing system in man, particularly in quoting it in justification of his advocacy of section of the chorda tympani.

F. W. Watkyn-Thomas

469. **Changes in Tympanic Cavity and Antrum Resulting from Radical Mastoid Operation**

H. BRUNNER. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **60**, 655–676, Dec., 1954. 11 figs.

The author describes the postoperative changes in the tympanic cavity and antrum in 11 patients (12 temporal bones), on all of whom a classic radical mastoidectomy had been performed, by postaural incision with curettage of the tubal orifice and hypotympanum and a Panse flap. The interval between operation and the patient's death ranged from a few hours to 21 years.

The author first stresses that the attic–antrum region behaves differently from the meso- and hypo-tympanum. In the attic and antrum after a successful operation there is no surviving mucosa and no cholesteatoma matrix. Granulation tissue, arising from the marrow spaces in about 3 weeks, changes to connective tissue and affords a base for the extension of epidermis from the plastic flap. When epidermization is complete, there lies between the epidermis and bone a layer of connective tissue, which may then shrink or may be invaded by a network of bone spicules. To achieve this result all osteitic bone must be removed, the outer attic wall removed up to the insertion of the malar, and the formation of granulation tissue controlled. It is not possible to make a smooth cavity of the meso- and hypotympanum on account of the anatomical arrangement. Further, epidermization depends largely on the nature of the epithelium of the area; for example, if before operation the area has been covered by squamous epithelium, parts of this are shed after operation and such a cavity can become fully healed. But if there is columnar epithelium the difficulty of healing is greater, since columnar epithelium is not spontaneously cast off, it is less resistant to infection from without than is squamous epithelium, and it extends more rapidly from the Eustachian tube into the mesotympanum than does the latter from the skin of the meatus. The author believes that this columnar epithelium is a more common cause of reinfection of a cavity than infection from the Eustachian tube and peritubal marrow spaces. In many cases he does not think it possible to close the tubal orifice into the mesotympanum or to remove all the columnar mucosa even with the aid of low-power magnification.

The cholesteatoma matrix should always be removed as far as possible. This is easy in the attic and antrum, but is neither possible nor necessary in the meso- and hypo-tympanum—it is not possible, even under magnification, because of the survival of shreds of matrix in the recesses of the windows—but it is not necessary because: (*a*) the need is greatest when there is underlying osteitis which, if advanced, results in eventual invasion of the labyrinth, and such a situation demands a labyrinth operation as well as the mastoid operation; (*b*) when there is not advanced osteitis there is spontaneous expulsion of the matrix from the wall of the mesotympanum after the mastoid operation.

Apart from minute cholesteatomata, which are not uncommon in epidermized cavities but generally do not expand or cause symptoms and usually discharge into the main cavity spontaneously, new formation of a cholesteatoma in a cavity is rare. Such a " recurrent " cholesteatoma differs from the exfoliation of necrotic epidermis. In genuine cholesteatoma of the cavity there is involvement of the underlying bone with destruction by osteoclasts and granulation tissue. The author regards such a cholesteatoma as a new formation and not as a real recurrence. He states that there is no proof that epidermis buried in a cavity gives rise to the formation of cholesteatoma. *F. W. Watkyn-Thomas*

Urogenital System

470. The Use of Pitressin as a Test of Renal Function
C. P. LOWTHER. *Glasgow Medical Journal* [*Glasg. med. J.*] **36**, 35–42, Feb., 1955. 12 refs.

The effect of "pitressin" on the specific gravity of the urine was compared with that of a 12-hour fast (the modified Fishberg test) in 83 healthy medical students aged 20 to 30 years at the Western Infirmary, Glasgow. At 9 a.m. on the first day, without previous preparation, the bladder was emptied and 10 units of pitressin was given by subcutaneous injection. Urine was collected at 10 a.m. and at 11 a.m. and the specific gravity of each specimen was determined; 6 subjects failed to provide a specimen at one hour and 3 failed at 2 hours. On the following day, after an overnight fast of 12 hours, a sample of urine was collected and the specific gravity determined. In 14·5% of instances after the pitressin test and in 28·9% after the fasting test there was failure to produce urine of specific gravity of 1·020 or higher. If urinary specific gravity of 1·020 or more is regarded as normal for these tests then in 65·1% of instances there was agreement between the two tests. In 24·1% of cases there was a normal response to pitressin but not to fasting, while in 10·8% there was a normal response to fasting but not to pitressin. In 4 instances the specific gravity of the urine was less than 1·020 after both tests. The principal side-effects of pitressin were pallor, hyperperistalsis, colic, precipitate bowel action, and torpor, in that order of frequency. Faintness and oxytocic effects were noted in 2 subjects and headache and vomiting were each noted once.

The author considers that the pitressin test is an efficient substitute for the Fishberg test, but he emphasizes the potential danger of pitressin in patients with coronary arterial disease. *K. G. Lowe*

471. Patterns of Protein Excretion by the Kidneys
S. E. KING. *Annals of Internal Medicine* [*Ann. intern. Med.*] **42**, 296–323, Feb., 1955. 9 figs., 47 refs.

Of 15,000 young recruits who had proteinuria in a casual specimen, 4,000 were admitted to hospital and subjected to special investigation. Using a "serial urine protein excretion test" and five specimens of urine, the author found that about one-third of the recruits had intermittent proteinuria, about one-fifth had constant proteinuria, and one-third had no proteinuria on re-examination. The incidence of renal disease in those with constant proteinuria was high. Patients with intermittent proteinuria were re-examined at intervals up to 3 years, and it was found that the condition persisted in almost 80%. A review of previous reports showed that proteinuria of this type was likely to persist for many years and was associated with decreased expectation of life. Intravenous urography in 56 cases of intermittent proteinuria in the present series revealed "major renal abnormalities" in 11; the author states that a history of lumbar pain with haematuria or pyuria was usual in this last group. There was an association between intermittent proteinuria and "vasomotor instability". The amount of protein excreted was usually less than 1 g. daily, but in some cases it was much more. The albumin: globulin ratio as determined by the Tiselius method was slightly under 3. The author believes that orthostatic patterns of proteinuria may be due to a number of renal disorders, including chronic nephritis and pyelitis.

D. A. K. Black

472. Urinary Amino Acid Excretion in Renal Disease, with Observations on the Fanconi Syndrome
W. LATHEM, K. BAKER, and S. E. BRADLEY. *American Journal of Medicine* [*Amer. J. Med.*] **18**, 249–258, Feb., 1955. 1 fig., 42 refs.

Normally, 98% of the amino-acid filtered by the glomerulus is reabsorbed in the tubules, so that only a small quantity appears in the urine. Defective reabsorption, with excessive aminoaciduria, has been shown to occur in the Fanconi syndrome and in hepatolenticular degeneration (Wilson's disease), and the accompanying glycosuria, hyperphosphaturia, and abnormal bicarbonate loss in the Fanconi syndrome and the occasional glycosuria in Wilson's disease indicate that other tubular reabsorptive mechanisms may be involved. The pathogenesis of this tubular dysfunction is obscure. Structural lesions in the tubules are not prominent, and aminoaciduria does not appear to occur in conditions such as chronic pyelonephritis or glomerulonephritis when tubular damage is excessive. However, Squire (*Brit. med. J.*, 1953, **2**, 1389; *Abstracts of World Medicine*, 1954, **15**, 507) found that aminoaciduria due to diminished tubular reabsorption was not uncommon in the nephrotic syndrome.

The present authors have determined amino-acid excretion qualitatively by paper partition chromatography after fasting and after the intravenous infusion of solutions of amino-acids in 15 patients with acute and chronic renal disease of various types and in 8 normal subjects at the Presbyterian Hospital (Columbia University), New York. [No case of the nephrotic syndrome was included.] The amino-acid mixture used was "aminosol", a partial acid hydrolysate of fibrin supplemented with tryptophane and methionine, the solution containing 25 g. of amino-acids in 500 ml. of water. After the ingestion of 500 ml. of water, urine was collected over a period of 1 to 3 hours. An infusion of 500 ml. of aminosol was then administered intravenously over 2 to 4 hours, urine being collected hourly throughout the period of infusion in a number of cases and all urine voided during the period of infusion being pooled in others. Urinary amino-acids were determined by a modification of the two-dimensional paper chromatographic method of William and Kirby (*Science*, 1948, **107**, 481) and by the small-paper technique of Dent (ibid., 1950, **112**, 621), urine containing protein being prepared by ultrafiltration through collodion sacs.

No significant defect in amino-acid reabsorption could be demonstrated in the fasting patients with acute and chronic renal disease, the urinary chromatographic patterns being consistently normal in all cases, irrespective of the nature of the underlying disease process or the degree of renal functional impairment, while the reabsorptive capacity of the renal tubular cells appeared to be undiminished, since less of the infused amino-acid was lost in the urine by these patients than by the healthy control subjects.

The urinary amino-acid pattern during fasting differed strikingly from the normal in a patient with the Fanconi syndrome and gross aminoaciduria in whom renal blood flow and filtration were undisturbed. However, a normal excretory response to the intravenous infusion of amino-acids was elicited in this patient, suggesting that the defect in tubular reabsorption may involve only a small proportion of the nephron population. No light was shed on the pathogenesis of the tubular lesion in Fanconi's syndrome, although the absence of aminoaciduria in patients with severe renal disease suggests that factors other than tubular damage may be involved.

E. Forrai

473. **The Uraemias**

G. M. BULL. *Lancet* [*Lancet*] **1**, 731–736 and 777–781, April 9 and 16, 1955. 17 figs., 28 refs.

474. **Cystic Disease of the Kidneys. A Study of Dynamics and Chemical Composition of Cyst Fluid**

N. S. BRICKER and J. F. PATTON. *American Journal of Medicine* [*Amer. J. Med.*] **18**, 207–219, Feb., 1955. 9 figs., 7 refs.

At Fitzsimons Army Hospital, Denver, Colorado, physiological studies were performed on the kidneys of 6 patients with polycystic renal disease and 4 with simple renal cysts, the kidneys in 9 cases being exposed *in situ* by laparotomy, while in the 10th case the study was carried out post mortem. Fluid was aspirated from the cysts of the exposed kidneys and, after an initial sampling, a single dose of inulin (or in some cases PAH) was administered intravenously. Further samples were taken at intervals from different cysts in the polycystic kidneys and from the single cysts in the simple cases. Simultaneously, venous blood samples were drawn for analysis, and in some cases urine was collected via indwelling bladder or ureteral catheters.

It was found that inulin entered the majority of cysts in the polycystic kidneys, but not into the simple cysts. Similar findings were obtained with PAH, except that small amounts of this substance appeared to enter the simple cysts. The concentration of creatinine in the superficial polycystic cysts approximated that in the plasma, but exceeded it in the deep cysts. Sodium, potassium, chloride, and total solute values exceeded plasma levels in the polycystic kidneys, whereas in the simple cysts only the sodium value was higher, the total solute concentration being similar to that of plasma. The reason for the higher concentration of electrolytes in the polycystic cysts is unknown. It is concluded that many polycystic cysts may be dynamically connected to active nephrons, but that simple cysts do not have this connexion. It is thought possible that cystic nephrons may contribute to the function of the kidney.

G. W. Csonka

475. **The Nephropathies of Periodic Disease.** (Les néphropathies de la maladie périodique)

R. CATTAN. *Presse médicale* [*Presse méd.*] **63**, 237–238, Feb. 19, 1955. 14 refs.

The concept of " periodic disease " as a distinct clinical entity characterized by recurrent attacks of fever, arthralgia, and abdominal pain has been upheld principally by French workers, among whom Mamou, with the present author (*Sem. Hôp. Paris*, 1952, **28**, 1062; *Abstracts of World Medicine*, 1952, **12**, 309), was the first to point out that chronic renal disease may occur as a complication. In this paper the author reports several cases illustrative of the various types of renal disease observed. He stresses the frequently familial nature of the disease, and points out that although it may remain benign for many years, renal complications are liable to develop at any stage. These may take the form of simple albuminuria, a fatal type of lipoid nephrosis supervening upon prolonged albuminuria or arising *de novo*, or chronic azotaemic nephritis. Less frequently the patient may suffer from repeated attacks of acute lumbar pain and haematuria. It is suggested that these renal complications resemble those produced in experimental animals by stimulation of the autonomic nerve supply of the kidney and by anaphylactic phenomena, and that the whole syndrome of periodic disease may be related to an antigen–antibody reaction

[The case histories are very poorly documented and the whole paper is consequently unconvincing.]

T. B. Begg

476. **Therapy of the Nephrotic Syndrome. Sodium Restriction, Dextran, and Corticotropin (ACTH) Alone or Combined with Nitrogen Mustard**

L. GREENMAN, F. A. WEIGAND, and T. S. DANOWSKI. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **89**, 169–181, Feb., 1955. 1 fig., 35 refs.

At the Pittsburgh Children's Hospital (University of Pittsburgh School of Medicine) 30 children suffering from the nephrotic syndrome were treated with ACTH (corticotrophin) in 25-mg. doses 6-hourly for a month and with a diet containing 2 to 9 mEq. of sodium, 150 mEq. of potassium, and 3 g. of protein per kg. body weight per day, together with supplementary iron and vitamins. In addition, 25 patients received 0·3 mg. of nitrogen mustard per kg., usually on the third day of treatment, and 18 received infusions of dextran or polyvinylpyrrolidone. An antibiotic, usually penicillin, was given throughout the period of treatment.

Of the 30 children, 22 appeared to be cured. This was attributed to the ACTH and the diet rather than to the other therapeutic measures, and the authors stress that the effect of ACTH was not only to promote diuresis—proteinuria was relieved and the biochemical findings in the blood returned to normal in the majority of cases.

Wilfrid Gaisford

Endocrinology

477. **The Action of Cocarboxylase on the Hypophysoadrenal System and on Lymphopoietic Tissues.** (Azione della cocarbossilasi sul sistema ipofiso-surrenale e sui parenchimi linfopoietici)
P. LARIZZA, A. NOTARIO, and D. MEDURI. *Minerva medica* [*Minerva med. (Torino)*] **2**, 1562–1576, Dec. 12, 1954. 34 figs., 35 refs.

Experiments were carried out at the University of Pavia in order to study the anti-asthmatic properties of cocarboxylase and the hypothesis that it has some action on the adrenal cortex.

A total of 80 guinea-pigs were divided into 8 groups of 10 each (5 males and 5 females), one of which acted as a control group while 5 of the others were given daily injections of 2·5, 5, 10, or 20 mg. of cocarboxylase for a period of 10 or 20 days, the total doses received by the 5 groups being 25, 50, 100, 100, and 200 mg. respectively. These animals were killed and examined 24 hours after the last dose. The remaining 20 animals were divided into 4 groups, which were given single injections of 2·5, 5, 10, and 50 mg. of cocarboxylase respectively and were killed 3 hours later. The pituitary and adrenal glands, the first part of the small intestine, the spleen, and the lymph nodes were examined microscopically and histochemically, and the bone marrow was also investigated histologically.

The findings are reported *in extenso*, the most important changes being those found in the adrenal glands, in which the zona fasciculata was reduced and the medulla compact, hyperplastic, and encroaching upon the cortex in the animals given the smaller and medium doses of cocarboxylase, the higher doses appearing not to produce such marked changes. Similarly after treatment with low doses the ascorbic acid content of the adrenal cortex was increased and with the higher doses it was diminished. The phosphatase activity of the cortex was diminished after treatment with medium doses (5 mg. daily), whereas both acid and alkaline phosphatase activity in the small intestine tended to be increased. After small and medium doses the pituitary gland showed an increase in number of the basophil, "Schiff-positive" cells, whereas the eosinophil cells were correspondingly diminished in number. The spleen showed a reduction in number of the follicles, with endarterial proliferation of the central vessels and hyperplasia of the connective tissue, after small and medium doses, and marked hyperplasia and hypertrophy of the follicles with the higher dosages (20 mg. daily).

Similar changes were found in the lymph nodes—hypoplastic follicles and dilatation of the sinuses with small dosage (2·5 mg. daily), and hyperplasia and hypertrophy with high dosage (20 mg. daily).

The authors point out that the total effect of prolonged injection of cocarboxylase in medium doses resembled that produced by cortisone, cortisone-like substances, and ACTH, and they discuss the significance of this finding at great length. They conclude that the anti-asthmatic action of cocarboxylase is due to its cortisone-like effect.

V. C. Medvei

478. **The Biological Properties of the Adrenocorticotrophic Hormone.** (Характеристика некоторых биологических свойств адренокортикотропного гормона)
I. A. ESKIN. *Проблемы Эндокринологии и Гормонотерапии* [*Problemy Endokr. Gormonoter.*] **1**, 52–59, No. 1, Jan.–Feb., 1955. 4 figs., 9 refs.

The effect of the adrenocorticotrophic hormone (ACTH) secreted by the anterior lobe of the pituitary gland on the function of the adrenal cortex has long been known, but the elucidation of its influence on the pituitary itself and on other parts of the endocrine system is not yet complete. At the Institute of Experimental Endocrinology, Moscow, the author has studied the direct and indirect effects of ACTH on the sexual development and growth of the female rat, and concludes that although it delays the growth and development of the ovaries and uterus, it does not do so by hindering the production of gonadotrophic hormones by the pituitary, as it also slows up the general growth of the body.

It was observed that when ACTH is administered over a long period the reaction of the adrenal and thyroid glands diminishes, presumably owing to development of some form of resistance to the hormone.

H. W. Swann

THYROID GLAND

479. **A New and Simple Test for Hyperthyroidism Employing L-Triiodothyronine and the Twenty-four-hour I-131 Uptake Method**
S. C. WERNER and M. SPOONER. *Bulletin of the New York Academy of Medicine* [*Bull. N.Y. Acad. Med.*] **31**, 137–145, Feb., 1955. 2 figs., 7 refs.

The 24-hour uptake of radioactive iodine (^{131}I) by the thyroid gland before and after giving 75 to 150 μg. of triiodothyronine daily by mouth for 8 days was studied at the Presbyterian Hospital (Columbia University), New York, in a control group of 48 patients who were without thyroid disease and in 48 patients with toxic goitre. In the control group a sharp decrease occurred in the uptake of ^{131}I, no value exceeding 20% being obtained, whereas in the group of goitrous patients no value below 35% occurred. Since before the administration of triiodothyronine these values in the two groups overlapped in about one-third of the cases it is suggested that the method might be used for clarifying the diagnosis in doubtful cases. It was also shown that the procedure was useful in differentiating cases of non-toxic diffuse from those of non-toxic nodular goitre, the

former giving a normal response to triiodothyronine but the latter showing no reduction in uptake of ^{131}I. It was also possible to identify patients with early eye changes as cases of Graves's disease although they were still euthyroid at the time of examination, since they exhibited an abnormal response to triiodothyronine. Treated patients in sustained remission reacted normally.

F. W. Chattaway

480. The Use of I^{131} in the Determination of Thyroid Functions

I. FEUER, E. DICKLER, G. J. FRIEDMAN, A. GEFFEN, H. R. MARCUS, L. VENET, and J. J. VORZIMER. *Metabolism* [*Metabolism*] **4**, 1–9, Jan., 1955. 3 figs., 11 refs.

If radioactive iodine (^{131}I) is administered to a patient the radioactivity of the plasma at any given time represents the sum of that due to free ^{131}I and that due to ^{131}I incorporated in thyroid hormone. Since the rate of removal of free ^{131}I by the thyroid gland and the rate of discharge of its hormone are much greater in the hyperthyroid than in the euthyroid state, a different curve should be obtained in the two conditions when the plasma radioactivity is plotted against the interval since the dose of ^{131}I was given. This was found to be the case, and the authors, from the Beth Israel Hospital, New York, describe an easy [but questionable] method of expressing the difference between these curves from the ratios of plasma activity at 4, 24, and 48 hours. A satisfactory differentiation was observed.

[The dosage of ^{131}I was high (120 to 150 microcuries), but if a scintillation counter were used this could be considerably reduced.] *G. A. Smart*

ADRENAL GLANDS

481. The Adrenocortical Response to Extensive Burns in Man

H. WILSON, J. R. LOVELACE, and J. D. HARDY. *Annals of Surgery* [*Ann. Surg.*] **141**, 175–184, Feb., 1955. 12 figs., 9 refs.

At the University of Tennessee and the John Gaston Hospital, Memphis, Tennessee, the authors investigated the magnitude and duration of increased adrenocortical activity in 12 patients aged 19 to 78 years who had suffered severe burns involving from 18 to 55% of the body surface area. A brief clinical history of each patient is given, together with tables of laboratory findings. Changes in adrenocortical function were followed by performing serial eosinophil counts and by determining the daily urinary excretion of corticoids and total neutral 17-ketosteroids.

From their findings the authors draw the following conclusions. The daily output of corticoids rises after an extensive burn; this rise may be maintained, or the level may return to normal, regardless of whether the patient recovers or not. The excretion of 17-ketosteroids, however, declines in cases of severe chronic burns, usually in relation to the worsening of the patient's clinical condition. The total peripheral eosinophil count falls to zero following the initial injury, but rises slowly with clinical improvement. A prolonged, severe depression of the count usually, though not invariably, indicates a poor prognosis. In the authors' opinion an eosinophil count of more than 50 cells per c.mm. early in the course of a burn is associated with a favourable prognosis in uncomplicated cases. The urinary output of adrenal corticoids and the eosinophil count are inversely related immediately after the injury, but later the corticoid output may fluctuate independently, suggesting that the eosinophil count is not wholly subject to adrenocortical control in conditions of chronic stress.

Nancy Gough

482. Differential Diagnosis of Adrenal Lesions by the Use of the Intravenous Administration of Hydrocortisone

A. SEGALOFF, D. GORDON, and B. N. HORWITT. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **45**, 219–227, Feb., 1955. 7 figs., 9 refs.

The value of intravenous administration of hydrocortisone in the diagnosis of adrenal lesions, particularly virilizing adrenal hyperplasia, is discussed with reference to the results obtained in patients at Tulane University School of Medicine, New Orleans. Hydrocortisone was given by continuous intravenous infusion to a total dose of 50 mg. in 24 hours or 100 mg. in 48 hours; in several cases 100 mg. of ACTH in 24 hours was administered in addition.

In 2 girls aged 17 years with primary amenorrhoea and hirsutism a fall in the urinary excretion of pregnanediol chromogen and of 17-ketosteroids was observed with hydrocortisone, and a rise in both with ACTH. In a 28-year-old woman with Cushing's syndrome caused by a malignant adrenal tumour there was no change with hydrocortisone, but with ACTH a slight fall in urinary excretion of pregnanediol chromogen and a rise in that of 17-ketosteroids were noted. *A. C. Crooke*

483. The Effect of Salicylate and of *para*-Aminobenzoate on the Eosinophil Response to ACTH

P. A. O'CONNELL, A. ROY, and B. F. MASSELL. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **229**, 150–160, Feb., 1955. 3 figs., 31 refs.

Since the advent of ACTH (corticotrophin) and cortisone, numerous attempts have been made to determine whether other drugs used in the treatment of the rheumatic disorders act, like ACTH, by stimulation of the adrenal cortex. The results are reported from the Children's Medical Center (Harvard Medical School), Boston, of a study of the effect on adrenal cortical function, as indicated by changes in the eosinophil count, of the administration of sodium salicylate and *para*-aminobenzoate to 132 patients convalescent from rheumatic fever, chorea, or mild rheumatoid arthritis. All but 3 were between 5 and 16 years old.

Neither of the drugs had any effect on the eosinophil count when given alone in various dosages, nor was any effect observed when both were given together in doses of 60 to 90 mg. of each per kg. body weight daily. However, the eosinopenic response to the injection of 12 units of ACTH in 6 doses at hourly intervals, which was not affected by the administration of either drug in

doses of 60 to 90 mg. per kg. daily, was significantly increased by the administration of 100 to 125 mg. of sodium salicylate per kg. daily or of both drugs together in doses of 60 to 90 mg. per kg. daily.

Oswald Savage

484. **Mechanism of Diurnal Eosinophil Rhythm in Man**
H. D. KAINE, H. S. SELTZER, and J. W. CONN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **45**, 247–252, Feb., 1955. 5 figs., 5 refs.

The authors, at the University of Michigan Medical School, Ann Arbor, attempted to determine whether the diurnal variation in the level of circulating eosinophils in healthy subjects—a variation which is not observed in patients with adrenocortical insufficiency—is a reflection of the diurnal fluctuations in plasma corticoid concentration or a result of changes in the degree of stress in the body during the day in the presence of reasonable amounts of circulating adrenal steroids. Cortisone was therefore administered by mouth at regular intervals throughout the 24 hours to 7 patients with Addison's disease. No diurnal variation in the eosinophil count was observed. When, however, 4 similar patients received a single dose of 25 mg. of cortisone by mouth at 6 a.m. diurnal fluctuations were recorded which were similar to those seen in healthy subjects. The authors conclude that the fluctuation in the level of circulating eosinophils reflects the diurnal variation in the level of plasma corticoids and, in particular, changes in the intensity of peripheral activity of 17-hydroxycorticoids.

A. C. Crooke

485. **Primary Aldosteronism, a New Clinical Syndrome**
J. W. CONN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **45**, 6–17, Jan., 1955. 7 figs., 15 refs.

In this paper from the University of Michigan Medical School, Ann Arbor, the author describes the case of a 34-year-old woman, who was eventually found to have an adrenocortical tumour, in whom certain abnormalities of electrolyte metabolism were present which were considered to be due to excessive secretion of aldosterone. She had suffered from intermittent attacks of muscular weakness and cramps for 7 years and had also had polyuria for several years; at the time of examination she had albuminuria without oedema, and Chvostek's and Trousseau's signs were present.

Laboratory investigations showed there to be an alkalosis associated with high blood potassium and sodium levels. The urinary excretion of 17-ketosteroids and 17-hydroxysteroids was normal, but there was an abnormally large quantity of sodium-retaining corticoid in the urine. Renal function was satisfactory apart from intermittent proteinuria and a fixed low urinary specific gravity which was not corrected by the administration of "pitressin". Further studies showed that the sweat and saliva contained abnormally large amounts of potassium and very low levels of sodium. Administration of potassium was followed by a further decrease in the sodium content of the sweat and saliva, a slight decrease in the alkalosis, and a rise in the serum potassium level to 3·3 mEq. per litre, but no more. It is suggested that a high potassium intake stimulated the secretion of aldosterone, with consequent resistance to further elevation of the serum potassium level.

Apart from the changes in electrolyte metabolism, the responses to the administration of ACTH (corticotrophin) and Compound F were quite normal. The patient was in negative potassium balance, and the potassium loss was increased by the administration of ACTH or Compound F, but only in proportion to the loss of nitrogen, whereas in normal subjects the loss of potassium in such circumstances is in excess of that of nitrogen. Compound F and ACTH gave rise to an initial retention of sodium and chloride, followed by a great excretion. This is reminiscent of the changes which occur in some cases of nephrosis and it is postulated that, in the presence of an excess of aldosterone, elevation of the 17-hydroxycorticoid level antagonizes the effect of aldosterone on the passage of sodium ions across cell membranes. In the normal subject there is an excretion of sodium and chloride when the excretion of 17-hydroxycorticoid is at its lowest level after the cessation of administration of Compound F or ACTH. In this patient there was sodium retention at this time, and it is suggested that the sodium-retaining corticoid was still being secreted when ACTH production was at least partially suppressed.

The author believes this to be a case of a new clinical syndrome which he calls "primary aldosteronism" and which is characterized by excessive urinary excretion of a sodium-retaining corticoid, hypokalaemia, hypernatraemia, alkalosis, and a defect in the reabsorption of water by the renal tubules. It is suggested that some cases of "potassium-loss nephritis" may be examples of primary aldosteronism. Further investigations following the removal of the adrenocortical tumour are in progress.

Charles Rolland

486. **Increased Aldosterone Output during Sodium Deprivation in Normal Men**
J. A. LUETSCHER and B. J. AXELRAD. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **87**, 650–653, Dec., 1954. 2 figs., 18 refs.

The authors, working at Stanford University School of Medicine, San Francisco, have studied the mechanism by which sodium output is reduced in response to sodium deprivation in man. It is known that adrenal cortical hormones can increase the reabsorption of sodium by the renal tubules, and the output of one of these hormones, aldosterone, appears to be inversely related to sodium excretion. In the present study renal function and the output of aldosterone, 17-ketosteroids, and 17-hydroxycorticosteroids were measured in 2 healthy men whose sodium intake was restricted to 11 mEq. a day for a period of 6 days.

The sodium and potassium output, creatinine and inulin clearance, and 17-ketosteroid and 17-hydroxycorticosteroid output were measured by standard techniques, while the aldosterone output was determined by bioassay after fractionation by paper chromatography, the result being expressed in terms of the dose of deoxy-

cortone acetate with equivalent sodium-retaining activity; the actual quantity of aldosterone present was then calculated on the assumption that aldosterone is 30 times more active than deoxycortone. Aldosterone excretion in healthy subjects taking a normal diet has been shown to range from 1·8 to 3·5 μg. daily.

In both the subjects studied the output of aldosterone rose as sodium excretion fell during the test period. No significant change was observed in the renal clearance of creatinine and inulin, indicating that glomerular filtration was unaffected. Similarly the output of 17-ketosteroids and 17-hydroxycorticosteroids remained unchanged, suggesting that regulation of the secretion of aldosterone is not mediated through pituitary corticotrophin. *Nancy Gough*

487. **Clinical Aspects of the Arthritis Provoked by Deoxycortone.** (Aspects cliniques des arthrites provoquées par la désoxycorticostérone)
L. DE GENNES, H. BRICAIRE, and J. VILLIAUMEY. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **22**, 1–9, Jan., 1955. 6 refs.

In this paper, which was read before the Ligue Française Contre le Rhumâtisme in November, 1954, the authors discuss the effect of administration of deoxycortone acetate (DCA) to patients with Addison's disease. Of 120 such patients treated with DCA, 26 developed joint symptoms, and of these, 6 complained of severe arthralgia in various joints, 16 developed polyarthritis similar to that of rheumatic fever, and 4 had painful contractures with severe limitation of movement. These disturbances developed within days or weeks of the start of treatment, whether DCA was given by multiple injections or by subcutaneous implantation. With cessation of such treatment there was a slow improvement in the joint condition. Recurrence could often be provoked by a further course of DCA. Cortisone helped to control the arthritic manifestations, and the authors consider that a good case can be made out for the use of cortisone instead of DCA in the management of these cases to prevent the occurrence of painful and disabling polyarthritis. A number of representative case histories are given. *G. W. Csonka*

DIABETES MELLITUS

488. **Infants of Diabetic Mothers. II. Studies on the Electrolyte Metabolism and the Effects of Starvation during the First Days of Life.** [In English]
R. ZETTERSTRÖM and B. ÅBERG. *Acta paediatrica* [*Acta paediat. (Uppsala)*] **44**, 1–16, Jan., 1955. 5 figs., 34 refs.

The mortality among the infants of diabetic mothers is high, and although the cause is not known, it is possibly related to the generalized oedema which is a striking feature in these infants. Treatment by withholding food and fluids during the first few days of life has been tried, and in this paper from Karolinska Sjukhuset, Stockholm, metabolic balance studies carried out during this period and during subsequent feeding are described. The blood sugar and serum electrolyte concentrations were normal at birth, and there was no risk of hypoglycaemia during the period of deprivation. There was a tendency to slight hyperchloraemic acidosis during the period of thirsting and fasting, but no fall in the serum potassium level was observed. Urinary excretion of sodium was marked and was roughly proportional to the degree of oedema. There was also urinary loss of chloride and potassium, but to a lesser degree. When milk was given there was marked retention of potassium, but sodium continued to be excreted, the infant remaining in negative sodium balance. The authors suggest that there is a surplus of intracellular sodium in these infants, possibly due to adrenocortical overactivity, associated with a deficiency of potassium. Early administration of potassium is necessary both to correct the deficiency and to hasten elimination of sodium. *A. Paton*

489. **The Amelioration of Diabetes Mellitus following Subtotal Gastrectomy**
M. N. FRIEDMAN, A. J. SANCETTA, and G. J. MAGOVERN. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **100**, 201–204, Feb., 1955. 11 refs.

Subtotal gastrectomy performed for duodenal ulceration in 3 diabetic patients at the Brooklyn Veterans Administration Hospital, New York, was followed by marked improvement in the diabetes as indicated by a reduction in glycosuria and decreased insulin requirements. [In one patient, however, the improvement is not very satisfactorily demonstrated.] The authors discount the possibility that the postoperative loss of weight was responsible for the improvement, because the latter was sudden and preceded the period of maximum weight reduction and the diabetic state did not deteriorate when weight was regained. Removal of the duodenal inflammation is also considered to be an unlikely explanation, because the improvement occurred in spite of the stress of the immediate postoperative period, "which was certainly equivalent to the bodily response" to the presence of an ulcer. In one patient, however, the insulin requirement rose during an attack of pneumonia and when laparotomy was subsequently performed for suspected duodenal fistula.

The authors discuss their findings in relation to the "steeple" type of glucose tolerance curve and accompanying intermittent glycosuria which are not infrequently encountered after subtotal gastrectomy. They tentatively suggest that the reduction in severity of the diabetic state in these patients may be related to the presence of a hyperglycaemic factor in cells of the gastric mucosa. This has been demonstrated in the dog, in which species there are argentophil cells in the gastric mucosa resembling the alpha cells of the pancreatic islets; similar cells have been found in the mucosa of the stomach and duodenum of human beings. *H.-J. B. Galbraith*

490. **Diabetogenic Pancreatitis Secondary to Duodenal Ulcer.** (Les pancréatites médicales diabétogènes secondaires à l'ulcère duodénal)
L. CANNAVÒ. *Diabète* [*Diabète*] **3**, 41–42, March–April, 1955. 2 figs.

The Rheumatic Diseases

491. Aminotripeptidase Content of Synovial Fluid in Arthritic Diseases

M. ZIFF, J. SIMSON, E. SCULL, A. SMITH, J. SHATTON, and D. MAINLAND. *Journal of Clinical Investigation* [*J. clin. Invest.*] **34**, 27–34, Jan., 1955. 3 figs., 10 refs.

The enzyme aminotripeptidase is widely distributed in the tissues, being especially richly concentrated in the leucocytes. In inflammatory reactions in a fluid-containing body space, such as the synovium, it might be expected that the amount of enzyme released by the dissolution of inflammatory cells and those of the lining membrane would be correlated with the degree of inflammation. On the basis of this theory the authors have measured the enzyme activity in articular fluid by the rate of hydrolysis of glycylglycylglycine in a " veronal " buffer at *p*H 7·8 and a temperature of 37° C., cell-free and unhaemolysed synovial fluid being obtained by centrifugation at 3,000 r.p.m. The activity was expressed as percentage hydrolysis of substrate per hour.

At New York University–Bellevue Medical Center, examination of 112 specimens of fluid from the knee-joints of 98 patients gave the following ranges. In 11 cases of degenerative joint disease it ranged from 1·4 to 6·9%; in 17 cases of acute rheumatic fever from 3·6 to 12·2%; in 31 of rheumatoid arthritis from 3·3 to 56·3%; in 5 of gonococcal arthritis from 5·7 to 13·0%; and in 16 of gout from 3·3 to 46·2%. Widely scattered and relatively high values were a feature of the findings in rheumatoid arthritis and to a lesser extent in gout. Statistical analysis showed a positive correlation between enzyme level and duration of symptoms, and a highly significant difference in the mean enzyme levels of the six groups. [There was a small group of miscellaneous diseases for which only a maximum figure of 42% is given.]

In degenerative joint disease and in rheumatic fever the level of aminotripeptidase in the serum was little different from that in the synovial fluid, but in cases of rheumatoid arthritis and gout the synovial levels ranged far in excess of that in the serum. There was only slight correlation between the leucocyte count and the enzyme level. It is pointed out that determination of the synovial enzyme level as a measure of the severity of the inflammation and as a means of differentiation of various types of joint disease shows good agreement with the results obtained by a study of the characteristics of the synovial fluid by other means, although admittedly some overlapping occurs. It is suggested therefore that, provided the duration of the condition is taken into account, determination of the enzyme level in the synovial fluid should be of some value in differential diagnosis. The lack of correlation with the leucocyte count suggests that the source of the enzyme is more closely associated with an extrusion or degradation of the synovial lining cells.

Harry Coke

ACUTE RHEUMATISM

492. Convalescence and Prophylaxis against Recurrence of Acute Articular Rheumatism in Children. (Convalescence et prophylaxie des crises de rhumatisme articulaire aigu chez l'enfant)

J. LABESSE, Y. DAGONET, L. POUJADE, and R. COURRAULT. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **48**, 94–118, Jan., 1955. 27 refs.

The authors first review the accepted evidence that acute articular rheumatism is a sequel of infection with *Streptococcus haemolyticus* Group A, usually of the throat or respiratory tract, and emphasize the infectivity and the familial tendency of the condition. During treatment the spread of infection and the risk of re-infection and superinfection (with another type of Group-A organism) must be combated, while during convalescence measures for prophylaxis and rehabilitation are essential.

Convalescence begins with the cessation of treatment with hormones and salicylates, and should be passed in a convalescent home to which the patient is sent directly from hospital without spending any time in his own home. At the Hôpital de La Roche-Guyon, which is a convalescent institution and is especially equipped for the reception of such cases, the condition of every child is assessed on admission and a swab of the throat taken, this being repeated weekly. The child is kept in bed until the temperature, pulse rate, and erythrocyte sedimentation rate (E.S.R.) are all normal and any cardiac condition has become stable. Prophylactic treatment is given daily throughout the stay, and is continued after discharge, in the form of sulphadiazine or penicillin, or both may be given in succession.

Any sign of reactivation of the disease is treated by return to strict bed rest, and aspirin is given in doses such as to produce a serum salicylate level of 30 to 35 mg. per 100 ml. In cases of re-infection penicillin (1,200,000 units daily for 5 days, then 600,000 units daily for 5 days) is used in preference to aureomycin. After discharge the parents are instructed as to the routine to be followed under medical supervision; the need for continuous protection with antibiotics is again stressed. After a quiescent period of 6 months games may be permitted unless a cardiac lesion is also present, when at least one year must elapse.

Among 49 children treated with 1 g. of sulphadiazine daily for 6 weeks and followed up for 8 months there were 2 relapses (4%); in 100 patients given 200,000 units of penicillin orally twice a day there were 6 minor recurrences after 6 months (6%); and in 20 treated with sulphadiazine and then penicillin there was one case of relapse (5%). For comparison, among 131 children in whom treatment had lapsed there were 74 recurrences (56%) during a follow-up period of 11 months. Prophylaxis

should continue until the age of 18, or possibly for life, in the case of associated cardiopathy. *V. Reade*

493. **Biological Studies during the Course of Rheumatic Fever: Collation of Clinical, Haematological, Electrophoretic, and Serological (Antistreptolysin O) Findings.** (Etudes biologiques au cours de la maladie de Bouillaud. Confrontations cliniques, hématologiques, électrophorétiques et sérologiques (anti-streptolysine O) au cours de l'évolution)

J. CHAPTAL, R. JEAN, C. CAMPO, D. ALRAM, and J. FRAISSE. *Archives françaises de pédiatrie* [*Arch. franç. Pédiat.*] **11**, 1055–1083, 1954. 3 figs., bibliography.

In 39 cases of rheumatic fever admitted to the Clinique des Maladies des Enfants, Montpellier, extensive laboratory investigations were performed throughout the illness, the course of which is described. In 15 cases the attack was mild and uncomplicated, 13 patients were more severely ill, with cardiac involvement, and 11 were gravely ill. The treatment consisted in administration of 150 to 200 mg. of cortisone daily for 10 to 18 days and of 1,000,000 units of penicillin daily. This was followed by intravenous or oral administration of salicylates and in some cases surgical eradication of oral focal sepsis. The blood count showed a neutrophil polymorphonuclear leucocytosis in one-third of the cases, a neutrophilia without leucocytosis in another third, and a normal leucocyte picture in the remaining third. There was no correlation between the gravity of the illness and the blood picture, except that in 4 cases showing a polymorphonuclear leucocytosis an oral septic focus was found.

Determination of the serum fibrinogen level gave variable results which were not related to the severity of the disease. The erythrocyte sedimentation rate (E.S.R.) was markedly raised, but the degree of increase was unrelated to the intensity of the illness. Treatment with cortisone reduced its level, but it was usually very slow in returning to normal. No characteristic modification of the electrophoretic pattern of the serum proteins was discernible, either in relation to the disease itself or to its fluctuations. The total albumin content was usually reduced and those of the α, α_2, and γ globulins increased, α_2 globulin taking especially long to revert to normal levels. The appearance of hyperglobulinaemia was taken to indicate a persistent infective focus, but such disturbances of the serum protein pattern as were present during the progress of the illness became normal when the attack was over. Cortisone had the effect of restoring the normal pattern more quickly, but this fact was not helpful in assessing prognosis.

The antistreptolysin titres were commonly raised, though not proportionally to the gravity of the fever, and in some cases they remained normal. The effect of cortisone on these titres was variable, but the performance of tonsillectomy led to a rapid fall in them. Even so, the combination of tonsillectomy, penicillin, salicylates, and cortisone was not necessarily followed by a return to normal titres for many months. In the authors' opinion the occurrence of hyperglobulinaemia suggests some alteration in connective tissue, and this was further confirmed by the finding of an increase in the serum glucoprotein content. Although, on the whole, treatment with penicillin and cortisone was followed by regression of the biological disturbances, as reflected in clinical and biochemical improvement, these drugs are not considered by the authors to have any specific curative effect. *G. W. Csonka*

494. **Results of the Hormone Treatment of Rheumatic Fever.** (Résultats du traitement hormonal de la maladie de Bouillaud)

P. MOZZICONACCI and M. K. CARAMANIAN. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **48**, 3–59, Jan., 1955. 43 figs., bibliography.

The authors give an account of the treatment with cortisone or corticotrophin (ACTH) of 267 children suffering from rheumatic fever. The maximum period of follow-up was 3 years. The cases were divided into three main groups. (I) 23 patients with severe cardiac involvement and constitutional disturbances; of these 17 recovered, 12 without recrudescence, and 6 died. (II) 131 patients with simple carditis, some with choreic signs, of whom 114 recovered without recurrence up to the time of writing, and 6 died. (III) 113 patients with acute articular rheumatism, and also in some cases chorea, of whom 12 suffered a relapse, but 111 were eventually discharged without sign of cardiac involvement and 2 developed persisting murmurs; in 100 of these cases no recurrence has been reported.

Cortisone was used in the majority of cases, being given in doses ranging from 100 mg. per day, up to age 5, to 200 mg. per day for those aged 10 to 15 years, either orally or intramuscularly. ACTH was reserved for severe cases, such as those of pancarditis, heart failure, and the " malignant " type of the disease in which urgent measures were required and the intravenous route therefore justified, in doses of 10 mg. per day given by slow infusion. Treatment was given for 15 days and then, if the erythrocyte sedimentation rate (E.S.R.) was not below 20 mm. in one hour, was continued for further periods each of 15 days up to 4 to 6 weeks, with fortnightly reassessment, until the E.S.R. fell to below 20 mm. At this juncture the hormone was replaced by aspirin in a dose of 0·1 to 0·15 g. per kg. body weight until the E.S.R. became normal, when a progressively decreasing dose of hormone was given for 10 more days. In addition, 3 g. of ammonium chloride was given daily along with the hormone. The use of heparin or ethyl biscoumacetate may have to be considered in cases of acute carditis, and in cases of cardiac failure the authors found it advisable to precede hormone therapy by digitalization for 24 to 48 hours. All patients were also given an intramuscular injection of 1,000,000 units of penicillin intramuscularly, and this was followed by 400,000 units daily by mouth.

The authors regard hormone treatment as the most effective weapon against acute rheumatic fever, and while the treatment is not curative, it does appear to check recrudescence and to diminish the incidence of cardiac involvement in the articular type of the disease. *V. Reade*

CHRONIC RHEUMATISM

495. **Phenylbutazone in Small Doses in the Treatment of Diseases of the Joints.** (Phenylbutazon i små doser i behandling af ledsygdomme)
E. TOPHØJ, P. BASTRUP-MADSEN, and P. BECHGAARD. *Ugeskrift for Læger* [*Ugeskr. Læg.*] **117**, 375–378, March 31, 1955. 18 refs.

496. **A Study of Gamma Globulin in Rheumatoid Arthritis**
J. H. VAUGHAN, A. ARMATO, J. C. GOLDTHWAIT, P. BRACHMAN, C. B. FAVOUR, and T. B. BAYLES. *Journal of Clinical Investigation* [*J. clin. Invest.*] **34**, 75–85, Jan., 1955. 4 figs., 18 refs.

In a study carried out at Harvard University Medical School, Boston, of the fate of serum proteins in patients with rheumatoid arthritis small groups of such patients and normal control subjects were given intravenous injections of gamma globulin and albumin derived from both rheumatoid arthritic and normal blood and labelled with radioactive iodine (^{131}I), its rate of disappearance from the blood stream being then observed. The elimination of both globulin and albumin was found to be more rapid in the rheumatoid patients, irrespective of the origin of the protein fraction, but otherwise the two groups showed little difference. In further experiments *in vitro* it was shown that both rheumatoid and normal joint tissues removed at operation took up labelled gamma globulin without any significant differences. From these and other experiments the authors conclude that there is no evidence to support the concept of a specific relationship between joint tissue and plasma gamma globulin in rheumatoid arthritis. *Harry Coke*

497. **A Clinical Trial of a Derivative of a Bile Salt in the Treatment of Rheumatoid Arthritis. A Preliminary Communication**
T. C. HIGHTON. *New Zealand Medical Journal* [*N.Z. med. J.*] **53**, 569–580, Dec., 1954. 1 fig., 11 refs.

After drawing attention to the clinical observation that an attack of infective hepatitis may induce a remission of rheumatoid arthritis, the author recalls the successful results obtained by Hench with intravenous injections of bile salts. At the Queen Elizabeth Hospital, Rotorua, 56 patients with rheumatoid arthritis were given an intramuscular injection of 200 mg. of sodium triketocholanic acid, a bile-salt derivative, twice a week. To counteract the irritant effect of the injection an equal volume of 2% procaine was added to the bile-salt preparation; this, however, was omitted from the injections given to patients known to be hypersensitive to procaine. Few side-effects were observed. Injection abscesses developed in some cases, and a sensation of premenstrual tension was experienced by some female patients when the injection was administered during the pre-ovulatory phase. Other side-effects were polyuria and pain in the right hypochondrium.

Injection of this bile-salt preparation produced no immediate dramatic effect, but in 36 patients improvement was observed about the third to the sixth weeks, and was progressive thereafter, except for attacks of "arthritis in miniature". Improvement was maintained for periods varying between 18 months and 3 years, but the author considers that the course of injections must be continued for at least 2 years. He believes that the results compare favourably with those obtained with ACTH and cortisone. *A. Garland*

498. **Bone Marrow in Rheumatoid Arthritis**
J. HOULI and H. MONTEIRO MARINHO. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **13**, 327–330, Dec., 1954. 23 refs.

The literature on the bone marrow in rheumatoid arthritis is briefly reviewed in this paper from the University of Brazil and the results of an investigation of the bone marrow in 20 patients are reported. [The authors do not mention the degree of cellularity of the biopsy specimens, but differential counts are tabulated.] No common pattern was observed, but the authors noted marrow eosinophilia in 7 cases and plasmocytosis in 5. There was no correlation between the plasma cell count of the marrow and the plasma protein changes [which, however, were determined by flocculation tests only]. The authors discuss at some length the history of the L.E. cell phenomenon. No L.E. cells were, however, found in the 15 cases investigated in their series.
Nigel Compston

499. **Hydrocortisone by the Oral Route in Rheumatoid Arthritis (Preliminary Clinical Study).** (Hydrocortisone par voie buccale dans la polyarthrite chronique évolutive (étude clinique préliminaire))
F. LAYANI and J. PEYRON. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **22**, 30–37, Jan., 1955. 2 refs.

The authors record and discuss their observations in 16 cases of rheumatoid arthritis treated with hydrocortisone free alcohol given orally; some of the patients were followed up for 6 months or more. The drug was given in an initial dose of 40 mg. daily, which was then modified from week to week until the minimum daily dose sufficient to give reasonable relief was determined, this usually ranging from 30 to 60 mg. per day. The clinical effect was similar to that of cortisone, but comparable results were obtained with smaller doses. The most striking feature was the absence of any important side-effects. The authors confirm that hydrocortisone free alcohol is superior to cortisone in such cases.
Kenneth Stone

500. **Comparative Results of Treatment with Oral Hydrocortisone and with Cortisone.** (Résultats thérapeutiques comparatifs de l'hydrocortisone buccale et de la cortisone)
S. DE SÈZE, N. DEBEYRE, and P. BORDIER. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **22**, 38–44, Jan., 1955. 10 refs.

The hydrocortisone acetate suspension given by injection for its local effect is but feebly soluble in water and body fluids, whereas the recently introduced oral preparation, hydrocortisone free alcohol, is some 35 times

more soluble in serum. In this study the authors compare the results achieved with oral hydrocortisone in the treatment of 31 patients with rheumatoid arthritis and 2 with ankylosing spondylitis, all of whom had previously been treated for periods varying from 4 months to 3 years with maintenance doses of cortisone. Initially the oral hydrocortisone was given in approximately the same dosage as cortisone. The progress of the patients was then reviewed at intervals of a fortnight, when the daily dose was reduced by 10 mg. at a time until signs of relapse appeared.

In only 2 cases was little or no change noted on substituting hydrocortisone, the other patients being definitely better than when under treatment with cortisone; improvement in some cases was rapid and spectacular. In all but one of 26 patients a raised erythrocyte sedimentation rate fell, in 9 cases to normal, on changing to oral hydrocortisone.

It was found that with 40 to 50 mg. of hydrocortisone the clinical and biological response was just superior to that with 75 mg. of cortisone—in other words, that hydrocortisone is 1½ times as active as cortisone. All the patients in this study had tolerated maintenance doses of cortisone without side-effects, but after the change to oral hydrocortisone 3 patients developed tachycardia and swelling of the face. As the authors point out, previous reports on the incidence of side-effects with oral hydrocortisone have been conflicting, Boland reporting a diminution or disappearance of such side-effects as oedema and " moon-face ", whereas West and Newns (*Lancet*, 1954, **2**, 168; *Abstracts of World Medicine*, 1954, **16**, 406) found the opposite. *Kenneth Stone*

501. **Evaluation of Prolonged Cortisone Therapy in Rheumatoid Arthritis. A Four-year Study**
J. J. Bunim, M. Ziff, and C. McEwen. *American Journal of Medicine* [*Amer. J. Med.*] **18**, 27–40, Jan., 1955. 7 figs., 11 refs.

The results obtained in 78 patients suffering from rheumatoid arthritis who were given cortisone for periods ranging from a few weeks to 4 years are reported from New York University College of Medicine. Of 71 patients treated for more than 6 weeks, 16 were in remission, 20 showed major improvement, 31 minor improvement, and 4 were unimproved or worse. This group included 31 males and 40 females, 35 of whom were over 50 and 10 were under 20 years of age. Before treatment started arthritis had been present for 12 months or under in 19 patients, for 1 to 10 years in 29, and over 10 years in 23. In 17 patients the disease was in the early, reversible, stage and in about half it was in an advanced stage. The average daily dosage of cortisone in all except 3 cases ranged from 25 to 100 mg.; in 3 patients given more than 100 mg. a day peptic ulcer developed, which perforated in 2 cases.

Analysing their results, the authors note that in 13 of 16 patients with remission the disease was in the reversible stage at the start of treatment. It was noteworthy that 7 of the 16 were between 10 and 29 years of age. In general, clinical improvement was paralleled by a fall in the erythrocyte sedimentation rate, but there were many exceptions. In the majority of patients subcutaneous nodules did not disappear during treatment, while in 2 patients new nodules developed for the first time. The most disconcerting objective finding was an increase in areas of bone destruction. Serial radiographs in 20 cases showed that areas of bone destruction were present in 14 at the beginning of treatment; in 8 of these the area increased, in 5 it was unchanged, and in one it was diminished. In the 6 cases in which there was no evidence of bone destruction before treatment osseous damage developed during administration of cortisone, although in 5 there was clinical and laboratory evidence of improvement. There were 6 deaths in the series, 5 of which were probably unrelated to cortisone therapy. The sixth patient died from a fulminating pneumococcal infection which was masked by cortisone.

The authors consider the results to indicate that cortisone is still a useful drug in the treatment of rheumatoid arthritis. *William Hughes*

502. **Effect of Cortisone in the Long-term Treatment of Rheumatoid Arthritis. Observation of Thirty-five Patients Over a Three-year Period**
E. C. Toone and R. Irby. *American Journal of Medicine* [*Amer. J. Med.*] **18**, 41–50, Jan., 1955. 3 figs., 21 refs.

The clinical course in 35 patients with rheumatoid arthritis who were given cortisone over a 3-year period is described in this paper from the Medical College of Virginia Hospitals, Richmond, Virginia. The ages of the patients (19 males and 16 females) ranged from 33 to 74 years. At the start of treatment the disease was classified as early in 2 cases only; in the majority it was advanced. The daily dosage of cortisone ranged from 50 to 150 mg. (average 75 mg.). The patients were treated in hospital at the beginning, the drug being given by intramuscular injection during this period. The immediate results were good in 34 cases. The long-term results, however, showed that none of the patients experienced complete remission of symptoms. At the end of 3 years only 11 patients had benefited sufficiently to continue taking cortisone, there being major improvement in 7 and minor improvement in 4. Of the remaining 24 patients in the series, 19 ceased treatment because of toxic reactions or absence of any improvement in symptoms. There were 5 deaths in the series, 4 attributable directly or indirectly to cortisone.

Toxic reactions, which were frequent and in 10 cases were sufficiently severe to necessitate discontinuance of the drug, included moon-face, oedema, obesity, osteoporosis, and gastrointestinal ulceration or haemorrhage. In 6 cases abscess of the buttock developed following the first injections. Severe psychosis was noted in 3 cases, and rapid progressive joint damage in 2. Summarizing their results, the authors stress the fact that only 11 of the patients thought it worth while to continue cortisone for 3 years. They consider that the drug should not be used as a routine, but should be confined to those cases in which other forms of treatment have failed. *William Hughes*

See also Physical Medicine, Abstract 504.

Physical Medicine

503. **The Use of Pathological and Unlocking Reflexes in the Rehabilitation of Spastics**
T. FAY. *American Journal of Physical Medicine* [*Amer. J. phys. Med.*] **33**, 347–352, Dec., 1954.

In this paper on rehabilitation in cases of spastic paraplegia the author states that there are many ways of making muscles work even when brain levels above the crus are destroyed. Simple reflexes may be initiated by deep or superficial stimuli, or spinal mass reflexes may be initiated, as seen in Babinski's sign, to make a single muscle or a group of muscles contract. By inducing some of these reactions once or twice a day spastic muscles may be improved in volume and function, with diminution in the spastic tone and posture disturbance. There are 36 such reflexes which can be utilized. Muscles can be unlocked by using reciprocal reflex mechanisms and correct patterns of movement (some of which are described in detail). It is suggested that to study movement patterns a small turtle should be observed " in the act of moving the anterior extremities in a progression pattern ". *J. B. Millard*

504. **Physiotherapy in Degenerative Rheumatism.** (Physiothérapie du rhumatisme dégénératif)
J. H. MARCHAND, J. CLAUTOUR, and R. DESPROGES-GOTTERON. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **22**, 45–53, Jan., 1955.

The authors discuss the physical treatment of degenerative joint disease, particularly cervical spondylosis with brachial neuralgia. Their first line of attack is *x*-ray therapy, which they consider to have an anti-inflammatory action and to be superior to any other form of treatment. The dosage, which should not exceed a total skin dose of 1,200 to 1,500 r spread over 3 or 4 weeks, is small enough to be free from any undesirable effects. The first dose, usually one of 100 r, provokes a temporary exacerbation of pain, coming on some 3 to 5 hours after irradiation and lasting about 2 hours. If this reaction is not excessive a second dose of 150 r is given 48 hours later, successive doses being at this level. In many cases this treatment is followed by complete and rapid relief and for some patients 2 or 3 treatments may suffice. In other cases the pain abates gradually during the month following the end of treatment.

When pain persists beyond this period the authors have recourse to the use of constant current, calcium ionization being employed for its sedative effect. For cervical stiffness persisting after pain has abated they use iodine ionization, the current being applied transversely through the neck. Examples of other types of arthrosis are discussed from the same point of view. Their treatment of sciatica follows the same general plan. They have found that relief of pain follows *x*-ray therapy in cases of osteoarthritis of the hip and knee and in subacromial bursitis. *Kenneth Stone*

505. **Role of Physical Medicine in Relief of Certain Pain Mechanisms of Shoulder**
A. S. RUSSEK. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 1575–1577, Dec. 25, 1954.

The author first points out that the nature of a lesion causing pain in the shoulder must be accurately diagnosed before treatment can be prescribed. He suggests that in 75% of patients shoulder pain is due either to postural stress or to adaptive changes in the shoulder and shoulder girdle secondary to some specific lesion. The scapulo-costal syndrome, with pain in the neck which may radiate down the arm and to the sternum, is the result of postural stress. When symptoms are chronic there is persistent spasm of the trapezius. This is often treated by application of heat and massage, but the effect of such measures is transient only. Treatment is aimed at the relief of muscle spasm, postural re-education, and relief of the persistent postural pull on the muscle.

Adaptive changes are associated with loss of movement in the gleno-humeral joint, which may follow many lesions in the shoulder-joint, including acute bursitis, fractures, and rheumatoid arthritis. Treatment consists in relief of muscle spasm and application of heat and massage, which, in the author's view, must be followed by passive movements to the point of tolerance and even beyond. He emphasizes the palliative value of physiotherapy as a preliminary to restoration of function.
W. Tegner

506. **A New Approach to the Treatment of Cervical Osteoarthritis with Radiculitis**
E. W. FOWLKS. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **35**, 765–772, Dec., 1954. 2 figs., 11 refs.

In this paper from the Veterans Administration Hospital, Portland, Oregon, the pathological anatomy of the cervical vertebrae, including the atlanto-axoid and the occipito-atlantoid articulations, is first discussed. It is then pointed out that the presenting symptom of cervical osteoarthritis is often referred pain leading in some instances to misdiagnosis of the condition.

From a wide experience of the treatment of cases of cervical osteoarthritis the author found that simple traction often induced considerable muscle spasm and was not, therefore, always successful. Electromyographic tracings showed that moist heat tended to reduce this spasm, and a combination of moist heat (in a cabinet) and traction was found to be a more effective therapeutic measure. In about 20% of over 300 cases some restriction of movement was still present after treatment, and for this the author used manipulation, the technique of which is described. *B. E. W. Mace*

See also Respiratory System, Abstract 466.

Neurology and Neurosurgery

507. **Language Laterality in Left-handed Aphasics**
H. GOODGLASS and F. A. QUADFASEL. *Brain* [*Brain*] 77, 521–548, 1954. 2 figs., bibliography.

The authors have examined 320 patients with aphasia at the Cushing General and the Boston Veterans Administration Hospitals, Boston, among whom they found 13 cases of left-handedness with unilateral lesion of the anatomical language area. In addition they have collected 110 similar cases reported in the literature. Of these 123 left-handed patients, 58 were " right-brained " for speech and 65 " left-brained ". Thus 53% failed to show the expected relationship between left-handedness and a dominant right hemisphere.

They discuss the differences between language laterality and handedness. It is well recognized that language laterality can change in childhood, but the authors consider it quite unproved that this change can take place in later life. They suggest that the tendency for language to centre predominantly in the left hemisphere is in large measure independent of handedness, and that this tendency is more nearly universal than the tendency to right-handedness. They point out that no theory of lateral specialization has yet been offered to account for the following facts. (1) Either hemisphere can function alone for language if the other is severely damaged early in life. (2) Aphasia due to right-sided lesions occurs more frequently in children than in adults. (3) In children aphasia is more often transitory. (4) Left-handed people are possibly more susceptible to aphasia from lesions of either hemisphere than are right-handed ones. (5) The specialization of the left hemisphere for language in most right-handers is much more extreme than specialization of either hemisphere in left-handers. (6) The period of consolidation of language laterality in childhood is one of increasing learning ability in both verbal and non-verbal areas; thus the consolidation does not constitute a cessation of learning ability.

N. S. Alcock

508. **The Value of Axon Responses in Determining the Site of Lesion in Traction Injuries of the Brachial Plexus**
G. BONNEY. *Brain* [*Brain*] 77, 588–609, 1954. 15 figs., 18 refs.

It has been suggested that in traction injuries to the brachial plexus part of the lesion may be an avulsion of nerve roots from the spinal cord. Working at the Institute of Orthopaedics, London, the author has therefore studied the axon reflexes in 13 cases of complete traction lesions of the brachial plexus by means of two methods: (1) the histamine response and (2) the cold vasodilatation response. In the first a 1-in-100 solution of histamine is pricked into the skin of the forearm and hand, the normal triple response being local vasodilatation followed by a weal and surrounded by a flare; the absence of the flare is considered abnormal. In the second method thermo-electric measurement of heat elimination from the fingertips is performed by means of heat-flow disks.

Of the 13 patients, the axon-reflex responses were absent in 4, and it was therefore assumed that the lesion was postganglionic. In 3 of these cases there was some degree of recovery, but in the fourth the plexus was torn across completely. The remaining 9 patients showed a positive axon-reflex response both to cold and to histamine. In these cases it was assumed that the lesion was preganglionic, that is, a lesion proximal to the posterior-root ganglion and probably intradural. In none of these patients was there any sensory recovery, and in only one any motor recovery. It is suggested, therefore, that the study of these reflexes may be of considerable value in determining the site of the lesion and in estimating the ultimate prognosis in such cases.

[Those interested in these methods should read the original paper, adequate details not being readily given in an abstract.] *N. S. Alcock*

DIAGNOSTIC METHODS

509. **Studies of the Electroencephalogram of Normal Children: Comparison of Visual and Automatic Frequency Analyses**
H. P. F. CORBIN and R. G. BICKFORD. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] 7, 15–28, Feb., 1955. 17 figs., 9 refs.

An attempt was made at the Mayo Clinic to assess the usefulness of the Walter electronic analyser in the interpretation of the electroencephalogram (EEG) of normal children, tracings being studied from 71 normal children whose ages were distributed fairly evenly from 1 to 10 years. The findings are described and the relative merits of visual and automatic analysis of EEG tracings are discussed.

It is pointed out that automatic analysis takes no account of artefacts, for which reason the leads used for comparison were those from the parieto-occipital regions and the analysis epochs were selected after consideration of the primary traces. Similarly, the analyser fails to indicate the presence of transients such as spikes which are so striking to the eye—and so important. Automatic analysis must, therefore, be additional to visual, and it is suggested that it may in fact provide the observer with more information than can be subjected to continuous visual analysis. On the other hand the analyser may be of great value when applied to physiological changes such as those associated with eye opening or overbreathing.

[The findings on which this paper is based are well set out and should be studied in the original. They form a valuable addition to the rather scanty precise informa-

tion on the frequency content of the EEG in this age group. It is noteworthy that the EEG in 4 cases showed gross abnormalities, which in 3 cases included focal sharp waves.] *W. A. Cobb*

510. **Metrazol and Combined Photic–Metrazol Activated Electroencephalography in Epileptic, Schizophrenic, Psychoneurotic, and Psychopathic Patients**
H. LEFFMAN and V. P. PERLO. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] 7, 61–66, Feb., 1955. 4 figs., 8 refs.

In a study of 150 patients at Madigan Army Hospital, Tacoma, Washington, the work of Gastaut on the myoclonic threshold with combined leptazol and photic stimulation was confirmed in that the threshold was found to be low in epileptics and in 53% of 53 schizophrenics, compared with only 2% of 50 psychoneurotics and psychopaths. The electroencephalographic response in epileptics was different from that of the other patients. [The illustrations fail to demonstrate the alleged difference.] In the schizophrenics the threshold was found to be temporarily raised by electric convulsion therapy.

[No description of the clinical material is given, but as the 150 patients came from a military hospital it may be supposed that they were highly selected in respect of sex, age, and initial neuro-psychiatric well-being. The results for leptazol stimulation and combined leptazol and photic stimulation are inextricably mixed; some are expressed in terms of exact dosage and others in the more rational form of dosage per kg. body weight. The accepted normal value for combined stimulation is not expressly stated, though it appears to be 7 mg. per kg., while for leptazol alone 400 mg. is stated to be a low threshold value.] *W. A. Cobb*

HEREDITARY DISORDERS

511. **Hereditary Sensory Neuropathy**
I. H. HELLER and P. ROBB. *Neurology* [*Neurology*] 5, 15–29, Jan., 1955. 7 figs., 43 refs.

Hereditary sensory neuropathy, which is transmitted as a Mendelian dominant character, causes gross peripheral sensory loss, loss of deep reflexes, and severe trophic lesions of all four extremities. The authors review the historical background of the condition since Nélaton's first description of "hereditary perforating ulcers of the feet" in 1852. Many cases have been reported since the turn of the century, and many theories propounded regarding the pathogenesis of the condition. In 1929 Guillain and Thévenard reported the cases of two siblings whose father, brother, and sister had died of a similar disease, and Thévenard and Coste reported a further two cases in 1935 from a different family. These patients had loss of pain and temperature sensation over the distal portions of the feet, with only slight impairment of touch. Position and vibration sense were intact. The deep tendon reflexes remained intact until late in the disease, when the ankle-jerks were diminished. Trophic ulceration of the feet developed, necessitating amputation, but the upper extremities, with one exception, were spared. In both these publications the authors favoured the diagnosis of familial lumbosacral syringomyelia, but Thévenard, in publishing a follow-up report in 1942, came to no definite conclusion about the nature of the condition, to which he applied the descriptive term *acropathie ulcéro-mutilante familiale*. In 1951 Denny-Brown reported the first necropsy on a patient suffering from hereditary perforating ulcers of the feet. This patient, a woman, was a member of a family first studied in 1922, of which many members were affected, with variations of the syndrome of deafness, shooting pains in the legs, peripheral sensory loss in the legs and later the hands, especially for pain and temperature, and perforating ulcers of the feet. No significant changes were found in the spinal cord or anterior roots, but there were definite changes in the dorsal root ganglia and afferent nerve trunks. There was severe loss of ganglion cells and degeneration of many of those remaining. There was also extensive demyelination of the peripheral nerves contributing to the ganglia. Denny-Brown described the condition as "hereditary sensory neuropathy".

The present authors, working at the Montreal Neurological Institute (McGill University), have studied a French-Canadian family and traced their pedigree back for 6 generations, there being 5 members with the classic disease, 4 of whom are living. In addition, there were 3 members who showed a mild, incomplete form, one of whom also showed evidence of intrinsic disease of the spinal cord, probably disseminated sclerosis.

The authors discuss the relationship between this syndrome and Morvan's disease in the light of Morvan's original descriptions, in which he attempted to make some distinction from syringomyelia. They consider that hereditary sensory neuropathy is due to a metabolic error transmitted by a dominant gene from generation to generation, and note a resemblance to the sensory neuropathy occurring in association with bronchogenic and other types of carcinoma. *J. MacD. Holmes*

CEREBRAL INFECTIONS

512. **Management of *Hemophilus influenzae*, Type B, Meningitis**
R. KOCH and M. J. CARSON. *Journal of Pediatrics* [*J. Pediat.*] 46, 18–29, Jan., 1955. 5 figs., 36 refs.

Between 1930 and 1953 128 cases of meningitis due to *Haemophilus influenzae* were treated at the Los Angeles Children's Hospital, and the analysis of these cases presented here reflects the spectacular advance made during this period in the treatment of this condition. The first 14 patients in the series received no specific treatment, none being available at that time, and all died within 2 weeks of admission. Of the second group of 13 children, who were treated with sulphonamides in doses up to 0·4 g. per kg. body weight per day, 2 survived, giving a case fatality rate of 85%. The 12 children in the third group were treated with rabbit antiserum against *H. influenzae* Type B combined with sulphonamides; 10 survived, of whom 2 had residual complica-

tions such as mental retardation, blindness, hydrocephalus, and convulsions, the case fatality rate in this group being 17%. When streptomycin was introduced in 1946 it was given combined with sulphonamides to 21 children, and in 6 other cases Type-B antiserum was added. As a result, the case fatality rate was further reduced to 7·4%, but the incidence of residual damage remained at 20%.

The position was considerably improved with the introduction of oxytetracycline in 1949, this antibiotic being used in combination with streptomycin and sulphonamides in 46 cases with only 2 deaths (4·3%), while an equal number of the survivors developed residual complications. Finally, among 16 patients who received chloramphenicol in various combinations with other antibacterial drugs the mortality was *nil*, residual damage occurring in one case. However, these patients were not treated according to a well-planned scheme, and the chloramphenicol was introduced at varying stages of the treatment. In spite of the fact that 75 cases have been reported in the literature to have been treated with chloramphenicol (alone or in combination with sulphadiazine) with a case fatality rate of 4%, residual damage in 8·3%, and no haematological complications, the authors are sceptical of the value of this drug as compared with their routine use of oxytetracycline, streptomycin, and sulphonamides.

One of the last patients in this series recovered from *H. influenzae* meningitis only to succumb to an overwhelming septicaemia due to drug-resistant haemolytic staphylococci, and it is emphasized that this danger of antibiotic therapy must be borne in mind.

K. Zinnemann

513. **Some Observations on Brain Abscess**

E. A. STUART, F. H. O'BRIEN, and W. J. MCNALLY. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **61**, 212–216, Feb., 1955. 9 refs.

A study is presented of 125 cases of brain abscess treated at the Montreal Neurological Institute and Royal Victoria Hospital, Montreal, during the 25 years 1925–50. Cases of abscess due to injury are excluded, and the authors note that the incidence of certain types of abscess—for example, abscesses secondary to acute frontal sinusitis—may be unusually high in this series, as many cases were referred from other hospitals. The conclusions which they reach may be quoted in full.

" (1) Infection of the ears and paranasal sinuses is the commonest source of intracranial abscess, and otitis media is the most frequent single cause. (2) Chronic more often than acute otitis media and mastoiditis results in intracranial abscess. (3) Intracerebral abscess as a complication of otitis media, is more frequent than intracerebellar abscess. (4) Intracerebellar abscess is almost invariably derived from primary infection in the middle ear. (5) Acute suppurative paranasal sinusitis with osteomyelitis is the second commonest source of intracerebral suppuration. (6) Infections of the lung are the most frequent sources of intracranial abscess derived from loci remote from the head. (7) Metastatic suppurations of the brain are frequently multiple, and are almost invariably located above the tentorium. (8) The apparent increase of cases of cerebral venous thrombosis may indicate that in some patients antibacterial therapy has arrested the progress of infection which might otherwise have gone on to brain abscess."

[This is a short but very useful paper.]

F. W. Watkyn-Thomas

CEREBRAL VASCULAR DISORDERS

514. **Studies on Headache. Variations in Fluid and Electrolyte Excretion in Association with Vascular Headache of Migraine Type**

W. W. SCHOTTSTAEDT and H. G. WOLFF. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **73**, 158–164, Feb., 1955. 2 figs., 6 refs.

The authors report the results of studies of fluid and electrolyte excretion carried out at the New York Hospital (Cornell University Medical College) before, during, and after 26 attacks of migraine in 8 subjects. The average rate of urinary flow before and during the early phases of the attack was 0·47 ml. per minute compared with an average of 1·44 ml. per minute during its subsidence. The average rate of sodium excretion before the attack was 47 μEq. per minute compared with 1·33 μEq. per minute during its subsidence, and of potassium excretion 26 μEq. per minute compared with 68 μEq. per minute. Major changes in creatinine excretion also occurred, the average rate of excretion being 0·738 mg. per minute before the headache and 1·044 mg. per minute afterwards; thus creatinine output is low before the attack but returns to normal as it subsides. Weight gain before the headache and weight loss afterwards were common, but not invariable. The authors conclude that fluid and electrolyte retention and alterations in renal circulation (as evidenced by creatinine excretion) are common before an attack of migraine and are followed by diuresis of water and electrolytes as the headache wanes. However, these changes do not appear to be causally related to the onset, intensity, or duration of the headache, as in individual cases the diuresis may occur before the onset of the attack, or may be induced, without preventing or influencing it, while in persons subject to migraine the injection of " pitressin ", which causes fluid retention, does not precipitate an attack. As similar changes in water and electrolyte metabolism occur under conditions of overwork and stress in normal subjects, the authors consider that they form part of the pattern of widespread bodily changes which occur in adaptation to stress, of which the attack of migraine is another feature.

John N. Walton

515. **Cerebral Thrombosis in Young Adults**

L. BERLIN, B. TUMARKIN, and H. L. MARTIN. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 162–166, Feb. 3, 1955. 1 fig., 9 refs.

The histories are recorded of 10 cases of acute cerebral vascular accident, generally giving rise to hemiplegia, in patients aged 13 to 34 treated at the Veterans Administration Hospital, Bronx, and the Bellevue Hospital

(Cornell University Medical College), New York, and mention is made of 3 others. Occlusion of the basilar artery was demonstrated in the only fatal case, while in 4 others occlusion or narrowing of the internal carotid artery was demonstrated by means of arteriography. In none of the remaining 8 cases was there any evidence of intracranial haemorrhage or of syphilis, blood dyscrasia, hypertension, diabetes, polyarteritis nodosa, or disseminated lupus erythematosus, and no source of emboli was discovered. The authors suggest that cerebral thrombosis resulting from atherosclerosis was the cause of the acute episode in each case. They believe that cerebral vascular accidents arising from this cause are more common in young people than is generally recognized. All the surviving patients showed marked improvement, and one was known to be alive 32 years after the acute episode; in only 2 cases did more than one attack occur. It is suggested that the prognosis of this type of attack is relatively good in young individuals.

John N. Walton

516. **The Controversial Use of Cervical Sympathetic Block in Apoplexy**

G. DE TAKATS. *Annals of Internal Medicine* [*Ann. intern. Med.*] **41**, 1196–1210, Dec., 1954. 7 figs., 40 refs.

In this paper from the University of Illinois College of Medicine the arguments for and against the use of sympathetic block in cases of apoplexy are summarized, and the concept of cerebral infarction without actual mechanical vascular obstruction is stressed. The author agrees that cases of stroke occurring in patients with brain tumour, or in association with subarachnoid, subdural, or intracerebral haemorrhage, are unsuitable for sympathetic block. In all other cases the pathological process is best regarded as a cerebral infarction. Although the Kety method of determining cerebral blood flow has been used to prove the futility of sympathetic block in apoplexy, the author feels that the demonstration is fallacious and that paralysis of the cerebral vasoconstrictor mechanism is of benefit to the ischaemic areas.

The results obtained in 55 of the author's own cases are then reviewed. The method and indications for sympathetic block are discussed and the technique of injection described and illustrated. The number of injections given varied from 1 to 10 daily, and in 2 cases a plastic catheter was left *in situ* in the vicinity of the cervical sympathetic chain for 5 and 7 days respectively. The immediate aim of the injection is to produce a Horner's syndrome, and if this does not develop within 10 to 15 minutes the injection should be repeated. Rare complications are accidental puncture of the pleura or of the spinal cord as a result of misdirection of the needle through the intervertebral foramen; a fatal case of the latter accident is mentioned, but in the present series there were no untoward incidents. Of the author's 55 patients, all of 14 with cerebral embolism and 19 of 41 with cerebral infarction showed improvement. These results are compared with other series in the literature in which improvement in proportions ranging from 0 to 96% of cases has been reported.

M.—M

In discussing the failures the author makes the following points. Sympathetic block can be of help only if (1) the infarct is surrounded by a zone of oedema and vasoparalysis, (2) the vessels are not unduly sclerotic, and (3) provided there is adequate collateral circulation via the circle of Willis. Further, a period of prolonged hypotension may impede the temporary revascularization of the infarcted area by sympathetic paralysis. The mechanism of relief is as yet not clearly understood. but the author suggests that the gratifying results obtained in certain cases justify the use of this technique which, even if it produces no marked benefit, at least does no harm.

L. A. Liversedge

DISSEMINATED SCLEROSIS

517. **Special Problems of Urinary Control in Patients with Multiple Sclerosis**

S. R. MUELLNER. *Journal of Urology* [*J. Urol.* (*Baltimore*)] **73**, 254–260, Feb., 1955. 5 figs., 7 refs.

In this paper from Beth Israel Hospital, Boston, the author discusses the problem of urinary incontinence in patients with disseminated sclerosis. In a previous communication (*J. Amer. med. Ass.*, 1954, **154**, 975; *Abstracts of World Medicine*, 1954, **16**, 329) he described the management of 85 cases, in most of which it was possible to control the frequency and urgency of micturition and incontinence by limitation of fluid intake to bare physiological needs, elimination of infection of the urinary tract, and the judicious use of anticholinergic drugs, especially atropine sulphate in doses of 1/150 grain (0·26 mg.).

In the present series of 8 cases, details of which are given, there were complicating factors affecting the lower urinary tract which had to be dealt with before the urinary symptoms could be brought under control. It is pointed out that the urinary symptoms associated with disseminated sclerosis may completely mask any additional disease process present, such as urinary calculus or enlarged prostate, and therefore a precise appraisal of the state of the bladder and urethra is necessary, as well as the removal of any disease factor, before the routine conservative treatment outlined above can be undertaken. The author emphasizes that sudden urinary retention is not uncommon in patients with disseminated sclerosis and may sometimes be frequent and prolonged. In these circumstances transurethral resection of the vesical neck is advocated; this was performed in 3 of the present cases with successful restoration of micturition.

D. P. McDonald

518. **Phenomenon of Relief by Flush in Multiple Sclerosis. Its Use as a Foundation for Therapy**

R. M. BRICKNER. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **73**, 232–240, Feb., 1955. 5 figs., 15 refs.

The author, working at the Mount Sinai Hospital, New York, has studied the effect of intermittent treatment with rapidly acting vasodilator drugs on 86 patients with disseminated sclerosis. The rationale of this treat-

ment lies in the author's observation that constriction of the retinal vessels may occur in many cases of the disease, and that the resultant visual symptoms can be relieved, at least temporarily, with vasodilator drugs. This phenomenon, which appears not to be confined to the visual symptoms, is termed " relief by flush ".

The drugs used included amyl nitrite (1 to 6 " whiffs "), carbon dioxide (5% and 10% in oxygen with rebreathing, usually at a rate of 3 litres per minute for 10 minutes), and histamine phosphate (1%, given by iontophoresis at 5 mA until a flush of the desired intensity was achieved), and the effect of these methods of treatment upon 264 symptomatic phenomena of the disease is described. Where the symptoms were of not more than 10 months' duration 90% were relieved, and if the symptom was of less than 6 weeks' duration the relief was usually permanent; the more long-standing symptoms generally returned at a variable time after treatment, but could again be relieved by repetition of the flush. Frequency of treatment was based upon the needs of the individual patient.

The author suggests that these findings provide the basis for a long-term programme of effective treatment for most cases of disseminated sclerosis which, with education of the patient, can generally be carried out at home.

[The author gives his reasons for excluding spontaneous remission, facilitation by practice, and psychological effects as the cause of the improvement which he observed, but his argument is not entirely convincing.]

John N. Walton

NEUROMUSCULAR DISEASE

519. **The Digestive Effects of Amyotrophic Lateral Sclerosis.** (Le retentissement digestif de la sclérose latérale amyotrophique)

G. Boudin, J. Barbizet, B. Hillemand, and J. Lote. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **31**, 7–14, Jan. 2, 1955. 10 figs., 24 refs.

Since section of the vagus nerve affects the tone and motility of the gastro-intestinal tract, the authors suggest that lesions of the vagal nuclei should have a similar result. In a study of 12 cases of amyotrophic lateral sclerosis by radiological examination after a barium meal 10 of the patients showed dilatation or hypotony of the oesophagus, stomach, and occasionally of the duodenum. In 6 of the 12 cases there was bulbar palsy, and 5 of these patients had marked disturbance of gastro-intestinal motility, but in the 6 without bulbar palsy these changes were less marked. None of the patients complained of gastro-intestinal symptoms.

Three patients, 2 of whom had bulbar palsy and marked radiological changes, died. In all 3 cases the alimentary tract was histologically normal [but the nerve plexuses were not examined]. The central nervous system showed the usual changes associated with motor neurone disease, the dorsal and ventral vagal nuclei being particularly affected in 2 cases of bulbar paralysis; in the case without evident bulbar palsy the dorsal nucleus showed some changes, but the ventral nucleus was normal. The authors claim that their hypothesis has been proved.

L. G. Kiloh

520. **Prostigmine-induced Muscle Weakness in Myasthenia Gravis Patients**

L. P. Rowland, M. C. Korengold, I. A. Jaffe, L. Berg, and G. M. Shy. *Neurology* [*Neurology*] **5**, 89–99, Feb., 1955. 8 figs., 27 refs.

Working at the National Institute of Neurological Diseases and Blindness, Bethesda, Maryland, the authors have studied the effects in 4 cases of myasthenia gravis of intravenous infusions of normal saline containing gradually increasing amounts of neostigmine methylsulphate. The initial dosage of the drug was 1 mg. per hour, and the concentration of the solution used was so adjusted that the average volume of fluid infused throughout was 100 ml. per hour, although this rate might be exceeded for short periods. Atropine sulphate was added to the solution usually in the proportion of 0·1 mg. for each 1 mg. of neostigmine, but care was taken to see that no patient received more than 2 mg. of atropine during a single infusion. Except in one case, neostigmine was withheld for 12 hours before each infusion. During the infusion grip strength was measured periodically with a dynamometer, and the period of time for which the arm could be held at shoulder level was recorded; other tests of muscle power were carried out where indicated.

In all 4 cases an increase in weakness was observed when a certain rate of infusion was reached. In 2 cases the diminution in strength—amounting to profound weakness in one of them—occurred after the administration of 8 mg. of the drug within 2¾ hours; in another case profound weakness developed after 20 mg. had been given in 3¼ hours, while the remaining patient, who was very ill before the infusion was given, was somewhat weaker after receiving 10 mg. in 1¼ hours. In this last case there was no initial response to neostigmine, but in the others the increase in weakness was preceded by improvement (partial in one case) in the muscles affected. The neostigmine-induced weakness usually involved both " myasthenic " muscles and muscles which had not previously been affected by the disease. Recovery was rapid when the infusion was stopped. There was some evidence that weakness was induced by a lower dosage of neostigmine in mild than in severe cases. The possible means by which neostigmine produces this effect are discussed. It is pointed out that although weakness is unlikely to be caused by the doses of neostigmine generally used in clinical practice, the potential danger of giving very high doses should be kept in mind in treating patients who respond poorly to normal doses.

John N. Walton

521. **Radioisotope Studies in Neuromuscular Disease. 2. Studies in Muscular Dystrophy and Myotonia Dystrophica with Sodium^{22} and Potassium^{42}**

W. H. Blahd, F. K. Bauer, R. L. Libby, and A. S. Rose. *Neurology* [*Neurology*] **5**, 201–207, March, 1955. 3 figs., 8 refs.

Psychiatry

522. **Carbohydrate Metabolism in Brain Disease. IV. Effect of Hydrocortisone and Corticotropin (ACTH) on the Metabolic Effects of Administered Glucose in Patients with Chronic Schizophrenic and Manic-depressive Psychoses**

D. H. HENNEMAN, M. D. ALTSCHULE, and R. M. GONCZ. *Archives of Internal Medicine* [*Arch. intern. Med.*] **95**, 241–246, Feb., 1955. 5 figs., 4 refs.

The changes in the blood concentrations of glucose and of lactic, pyruvic, citric, and α-ketoglutaric acids after administration of glucose were studied in 4 patients with chronic manic-depressive or schizophrenic psychoses; all 4 patients showed abnormal utilization of the glucose in a pattern previously shown to occur commonly in chronic psychoses. Administration of hydrocortisone (3 cases) or corticotropin (1 case) for 3 days prior to the administration of glucose altered this pattern of disordered glucose metabolism so that the changes observed resembled those more commonly found in patients with psychoses of recent onset. The significance of these findings is discussed.—[Authors' summary.]

523. **Glutamic Acid in the Treatment of Mental Deficiency**

J. N. LEEDHAM. *Medical Officer* [*Med. Offr*] **93**, 117–122, 133–137, March 4 and 11, 1955. 1 fig., 28 refs.

A controlled trial of the effect of glutamic acid on the intelligence quotient of selected mental defectives attending the Occupation Centre, Bradford, is reported. From about 100 children 12 matched pairs aged 4½ to 17¼ years with mental ages ranging from 2 years 11 months to 7 years 7 months, were selected, one child from each pair serving as a control. Before and after the trial the following intelligence tests were carried out: the Revised Stanford–Binet Form L, Seguin's Form Board, the Progressive Matrices A, Ab, and B, and Crichton's Vocabulary Scale. Each child in the experimental group was given 10 g. of glutamic acid daily in powder form for 6 months, the control group receiving a similar quantity of saccharine lactate.

In both groups there was some deterioration in the intelligence quotient over the period of the trial, but there was no significant difference between the two groups, except perhaps that on retesting the experimental group did rather better at the Form Board than the controls. This suggested an increase in manipulative skill, a result not claimed by previous workers. Other claims by earlier workers—such as a decrease in the severity of the stigmata of mongols—could not be substantiated. There appeared to be some increase of "vitality and energy" in the controls.

A review and criticism of earlier studies of the effects of glutamic acid in the treatment of mental deficiency are appended. *L. G. Kiloh*

524. **Treatment of Phenylketonuria with a Diet Low in Phenylalanine**

L. I. WOOLF, R. GRIFFITHS, and A. MONCRIEFF. *British Medical Journal* [*Brit. med. J.*] **1**, 57–64, Jan. 8, 1955. 1 fig., 16 refs.

On the hypothesis that the mental deficiency of phenylketonuria is due to the toxic action of phenylalanine or of one of its metabolites, which constantly inhibits cerebral function without leading to irreversible damage of brain tissue, the authors, at the Hospital for Sick Children, London, gave a diet which was low in phenylalanine to 3 phenylketonuric children (2 idiots and one imbecile). The main protein constituent of the diet (which is stated to be "economically practicable") was an acid hydrolysate of casein that had been passed through a column of charcoal. The mental age of each patient was determined before, and at intervals after, starting the diet, which was given for 4½ to 10 months. The resulting steady increase in the mental age and I.Q. of all 3 patients supported the validity of the original hypothesis and raised hopes that these children might eventually prove educable. In one case attacks of petit mal ceased and the electroencephalogram became normal. *F. K. Taylor*

525. **Electroencephalograms during Cycles of Addiction to Barbiturates in Man**

A. WILKER, H. F. FRASER, H. ISBELL, and F. T. PESCOR. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **7**, 1–13, Feb., 1955. 1 fig., 22 refs.

At the U.S. Public Health Service Hospital, Lexington, Kentucky, two groups of former drug addicts were studied during and after the prolonged administration of quinalbarbitone. The members of the first group took a daily dose of 0·9 to 2·6 g. for up to 89 days, while the dose for the second group did not exceed 0·8 g. The subjects taking the larger doses showed considerable disturbance of affect and judgement and were ataxic and dysarthric; with constant dosage tolerance tended to develop, but the symptoms were restored by a very small increase. In the second group the effects were similar, though far less pronounced. In the latter group the electroencephalographic changes were mainly those of the familiar fast response to a barbiturate, but in the former there was also slow activity, mainly frontal and parietal; tolerance effects were not noticeable.

On sudden withdrawal of the barbiturate the symptoms rapidly disappeared, but generalized fits, 1 to 4 in number, occurred in 11 of the 14 subjects in the first group on the second or third day, and nearly all the subjects suffered anxiety, anorexia and loss of weight, insomnia, and tremulousness. Between the fourth and seventh days a majority became psychotic, being usually agitated, delirious, and hallucinated, for a few days. In the

second group the symptoms were much milder and only 2 subjects out of 21 had fits. The electroencephalograms of the first group were very abnormal, with "hypersynchrony", spikes and slow waves, and spike-and-dome discharges at 4 c.p.s. They did not reveal any clear correlation with the clinical condition, but tended to be more abnormal than those obtained in the second group. *W. A. Cobb*

TREATMENT

526. **Clinical Observations on "Megaphen" Treatment in Psychiatry.** (Klinische Beobachtungen bei Megaphenbehandlung in der Psychiatrie)
E. B. GÄDE and K. HEINRICH. *Nervenarzt* [*Nervenarzt*] **26**, 49–54, Feb. 20, 1955. 16 refs.

The authors describe the results of treatment with "megaphen", a phenothiazine derivative, of 160 patients seen at the University Neurological Clinic, Mainz, with mainly psychiatric disorders. Good results were obtained in cases of paranoid schizophrenia and cyclothymic depression, especially when megaphen treatment was combined with electric convulsion therapy (E.C.T.). They found that psychotherapy in patients with psychopathic personalities was also more efficacious when megaphen had been given. The drug was also of value in cases of alcoholic delirium and other toxic psychoses, while relief from pain, sometimes continuing after cessation of the treatment, was seen in cases of trigeminal neuralgia and root pains.

The side-effects of the drug included toxic exanthemata, lowering of blood pressure, jaundice, the appearance of a Parkinsonian syndrome, and also secretion from the mammary glands in 3 female patients, but none of these manifestations was permanent. The authors suggest that it may be possible to employ megaphen in place of insulin and E.C.T. in the treatment of the endogenous psychoses, with consequent lessening of risk and easier management of the patient. *J. B. Stanton*

527. **The Potentialities of "Megaphen" in Psychiatric Practice and Research.** (Anwendungsmöglichkeiten des Megaphens in der psychiatrischen Klinik und Forschung)
H. VON DITFURTH. *Nervenarzt* [*Nervenarzt*] **26**, 54–59, Feb. 20, 1955. 13 refs.

Writing from the University Neurological Clinic, Würzburg, the author describes the potentialities of "megaphen" as observed in the treatment of 10 patients with typical mania, 51 with endogenous depression, 23 with schizophrenia, 3 with psychopathic states, 7 with senile psychoses, 5 in alcoholic delirium, 9 in a paranoid state, and various other disorders, including some cases of drug addiction and epilepsy. The general psychological effects of megaphen and its side-effects are discussed.

The author suggests that the Parkinsonian syndrome which may be noted, if carefully looked for, in most patients receiving the drug is not strictly a complication, but is rather the organic manifestation (on the corpus striatum) of the effect of megaphen, running parallel with its influence in the psychological sphere. He concludes that administration of megaphen is a useful symptomatic treatment for affective disturbances and for secondary symptoms of emotional origin in the endogenous psychoses. In contrast to other observers, he did not find any consistent benefit in cases of endogenous depression. *J. B. Stanton*

528. **Experience with "Megaphen" in the Treatment of Psychiatric Patients.** (Erfahrungen mit Megaphen in der Behandlung psychisch Erkrankter)
E. PHILLIP. *Nervenarzt* [*Nervenarzt*] **26**, 59–65, Feb. 20, 1955. 4 refs.

This paper presents the author's experience at Waldhaus Nerve Clinic, Berlin–Nikolassee, with the use of "megaphen" in the treatment of 159 psychiatric patients. He concludes that treatment with megaphen cannot cut short the course of a psychosis, and that it cannot replace insulin or electric convulsion therapy or ensure a higher recovery rate in endogenous psychoses, but that it may be able to alter the psychopathological symtomatology. In his view megaphen is a useful drug in the symptomatic treatment of excited and anxiety states and for bringing about a temporary diminution in intensity of hallucinations. *J. B. Stanton*

529. **Therapeutic Results with Chlorpromazine ("Largactil") in Psychiatric Conditions**
H. E. LEHMANN. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **72**, 91–99, Jan. 15, 1955. 13 refs.

The therapeutic effects of chlorpromazine in a first series of 71 psychiatric patients at the Verdun Protestant Hospital, Montreal, have already been described (*Arch. Neurol. Psychiat.* (*Chicago*), 1954, **71**, 227; *Abstracts of World Medicine*, 1954, **16**, 156). The series has been extended since that time and in the present paper the results obtained in a total of 283 such patients are reviewed.

The drug was found to be particularly valuable for its symptomatic effect in all states of psychomotor excitement, including those associated with organic cerebral disturbances, in which it produced adequate sedation without either clouding of consciousness or disinhibition of affect. Direct therapeutic effects were most marked in manic-depressive psychosis—complete remission being obtained in 37 out of 77 patients in 40 days—and in schizophrenia—15 out of 54 patients whose symptoms had been present for one month or less recovering completely. Chlorpromazine was effective in shortening the duration of recurrent psychotic attacks, the difference between the mean duration of early attacks and that of episodes recurring after chlorpromazine had been used in treatment being statistically significant. In acute cases the drug was given by intramuscular injection for a week, after which oral administration was substituted. In the author's view the drug should be tried for 2 to 4 weeks before shock therapy is considered. Complications, which included hypotension, allergic manifestations, extrapyramidal syndrome, convulsions, and jaundice, are discussed, and some of the literature is reviewed in the light of the author's own experience. *A. C. Tait*

Dermatology

530. **Treatment of Vitiligo with Psoralen Derivatives**
W. M. GEORGE and J. W. BURKS. *Archives of Dermatology* [*Arch. Derm. (Chicago)*] **71**, 14–18, Jan., 1955. 24 refs.

The clinical study here reported from the Charity Hospital (Tulane University School of Medicine), New Orleans, was undertaken in an attempt to find an effective but safe method of treating vitiligo with the psoralen derivatives without causing undesirable side-effects. The drugs were given by mouth in daily doses of 0·7 mg. of 8-methoxypsoralen together with half that quantity of 8-*iso*amylenepsoralen or applied locally in a water-soluble ointment base, ointments containing 1, 2, and 3·5 g. of the former and half those amounts of the latter drug being used. Of 11 negro patients treated over a period of 4 weeks to 5 months, 7 received treatment with ointment alone, in increasing strength if no irritation occurred, and the other 4 received oral therapy as well. Application of the ointment was followed by exposure to sunlight, the ointment then being washed off. The results obtained are tabulated and discussed. The authors hope that the relatively good results obtained with both methods will stimulate others to use and to improve this method of treatment, and to investigate the exact mechanism by which the psoralen derivatives cause pigmentation. *G. B. Mitchell-Heggs*

531. **Hydrocortisone Ointment in the Eczemas**
R. CHURCH. *British Medical Journal* [*Brit. med. J.*] 1, 517–519, Feb. 26, 1955. 10 refs.

At the Royal Infirmary, Sheffield, a series of patients with various types of eczema and dermatitis were treated by application of an ointment containing 1% hydrocortisone acetate (in a few of the more resistant cases 2½% hydrocortisone was used), the base consisting of anhydrous lanolin, petrolatum, and mineral oil. A further 23 patients with eczema served as controls, alternate patients being issued at the beginning of the trial with the ointment base in a similar packing.

Improvement or complete healing was observed in 80 out of 105 treated patients and in 4 of the 23 controls. Improvement was most rapid in patients with a raw, weeping area of skin which allowed rapid absorption of the hydrocortisone. This method of treatment was notably beneficial in cases of acute contact dermatitis, nummular eczema, and pruritus ani with excoriation. On cessation of treatment the condition relapsed in some cases, especially in those of " atopic " eczema.
S. T. Anning

532. **Tinea Capitis. An Epidemiologic, Therapeutic and Laboratory Investigation of 6,390 Cases**
A. DOSTROVSKY, G. KALLNER, F. RAUBITSCHEK, and F. SAGHER. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **24**, 195–200, March, 1955. 17 refs.

533. **Successful Treatment of Acrodermatitis Atrophicans (Herxheimer) with Aureomycin and Oxytetracycline and its Aetiological Significance.** (Erfolgreiche Aureomycin- und Terramycinbehandlung als Beitrag zur Klärung der Wirkungsweise von Penicillin bei der Akrodermatitis atrophicans Herxheimer)
E. LUDWIG. *Dermatologische Wochenschrift* [*Derm. Wschr.*] **131**, 169–178, 1955. 2 figs., 21 refs.

When it became known that acrodermatitis atrophicans was amenable to penicillin therapy it was thought by some that this was due to the antibiotic properties of the drug acting on a chronic inflammatory process of uncertain aetiology. Others, including the author, believed the therapeutic success to be due to the influence of penicillin preparations on the vegetative nervous system. To help decide the issue, 11 patients were treated at the University Skin Clinic, Hamburg–Eppendorf, with aureomycin or oxytetracycline, which have no action on the vegetative nervous system; in 9 of the 11 cases, very good results were achieved. It is therefore concluded that the antibiotic properties of the effective preparations alone are of importance, thus strengthening the case for an infective aetiology in acrodermatitis atrophicans. *G. W. Csonka*

534. **Bullous Prurigo.** (Le prurigo bulleux)
A. CARTEAUD, J. HEWITT, and J. TABERNAT. *Presse médicale* [*Presse méd.*] **63**, 186–188, Feb. 9, 1955. 4 figs., 7 refs.

Bullous prurigo, although long ago recognized as a disease entity, now seems to be rarely diagnosed. After a brief review of some of the literature relating to the occurrence of bullae with prurigo in children, the authors discuss their observations on 16 cases seen in Paris during the past few years. (The paper is illustrated with clinical photographs and photomicrographs.)

The occurrence of bullae in prurigo is a comparatively uncommon manifestation. It is seen most frequently between the ages of 18 months and 3 years, the youngest patient in the present series being aged 15 months and the oldest 5 years. The bullae, which arise on normal skin and do not show an inflammatory areola, are usually 8 to 10 mm. in diameter, but may vary between 2 and 40 mm. They are not numerous and have no specific distribution, although perhaps they are most common on the posterior and lateral surfaces of the legs and on the soles of the feet. They are usually tense and contain clear fluid, unless infection supervenes. The duration of the eruption is usually from 10 days to one month; it may be recurrent, running a course like papular urticaria, which it much resembles. Irritation is rarely severe. No specific factors in aetiology were noted in the authors' cases, except perhaps some association with the ingestion of chocolate. Histologically the lesions show an intra-epidermal multilocular bulla, with an acute

general and perivascular infiltration with neutrophil and eosinophil granulocytes, oedema of the collagen substance, and some fibrinoid necrosis of the ground substance. The cytodiagnostic technique of Tzanck does not show any specific feature.

The chief interest of the condition lies in its diagnosis, and the authors discuss its differentiation from syphilitic pemphigus, epidemic pemphigus of the newborn, impetigo, epidermolysis bullosa, insect bites, solar eruptions, meadow-grass dermatitis, bullous drug eruptions, and the dermatitis herpetiformis of Dühring. Treatment consisted in the avoidance of starchy and fermentable foods, and good results were obtained from the administration of an extract of artichoke together with the use of local antipruritics. Antihistaminics were found to be of little value. *Benjamin Schwartz*

535. **Treatment of Psoriasis with Goeckerman Technic**
W. M. SOLOMON, E. W. NETHERTON, P. A. NELSON, and W. J. ZIETER. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **36**, 74–77, Feb., 1955. 7 refs.

The authors briefly review the recognized and characteristic features of psoriasis and refer to Mayr's finding that in the case of identical twins, where one is affected with psoriasis the other sibling is commonly affected. They state that the most satisfactory treatment is application of crude coal-tar ointment combined with ultraviolet irradiation, as described by Goeckerman in 1925, though this necessitates a stay in hospital. At the Cleveland Clinic 60 patients were treated by this method over a period of 2 years. There was marked improvement in the appearance of the skin in 56 cases. It is pointed out that general therapeutic measures are as essential in the successful treatment of psoriasis as in any other disease. A number of empirical remedies which have been recommended, including typhoid vaccine, gold salts, arsenicals, and, more recently, cortisone and corticotrophin, are discussed. *John T. Ingram*

536. **Radioactive Cobalt in the Treatment of Skin Tumours and the Use of Radioactive Threads in Cavernous Angiomata Near the Eye.** (Radioaktives Kobalt bei Hauttumoren und Hinweis auf Verwendung des strahlenden Fadens bei Kavernomen in Augennähe)
H. J. ENDRES. *Dermatologische Wochenschrift* [*Derm. Wschr.*] **131**, 145–151, 1955. 14 figs., 7 refs.

In the method of treatment here described from the University Skin Clinic, Heidelberg, radioactive cobalt (^{60}Co) is incorporated in small hard balls 2 mm. in diameter which are evenly distributed and fixed in a readily mouldable plastic material, thus ensuring easy application. Owing to the physical nature of this preparation it is possible to irradiate irregular surfaces evenly. As the author points out, this is much more difficult to achieve with the customary radium applicators —which are also more expensive. The preparation (" plastobalt-M ") can be shaped easily to such complicated surfaces as the outer ear, the oral cavity, and the nasolabial fold. The method has been used in the treatment of 22 patients, most of whom had basal-cell carcinoma or epithelioma. It is claimed that one or two sessions, during which a total dose of 2,500 to 4,500 r was given, resulted in disappearance of the growths. No recurrences have been observed so far during a maximum period of observation of 18 months.

A different method is described for the treatment of cases of cavernous angioma near the eye. In this, threads of collagenous material impregnated with radioactive phosphorus are introduced into the tumour. The β rays penetrate to a depth of approximately 2 mm. The preparation has a half-life of 14 days, and the inert thread is eventually absorbed. Four patients have been so treated, but too recently to allow of any definite conclusions; the results in one case seem promising.
G. W. Csonka

537. **Melanotic Freckle (Hutchison), *Melanose Circonscrite Précancéreuse* (Dubreuilh)**
J. V. KLAUDER and H. BEERMAN. *Archives of Dermatology* [*Arch. Derm. (Chicago)*] **71**, 2–10, Jan., 1955. 5 figs., 17 refs.

In discussing the type of malignant melanoma which arises from the pigmented lesion first described by Hutchison as the senile freckle or infective melanotic freckle, the authors stress the importance, from the standpoints of both prognosis and treatment, of differentiating it from the more serious type of malignant melanoma arising from the pigmented dermo-epidermal naevus.

The clinical features of the former condition, its histopathology, mode of spread, slowness of dissemination, and treatment are discussed and 5 cases are reported.
G. B. Mitchell-Heggs

538. **Fallacy of Term " Self-healing Epidermoid Carcinoma " and Limitations of Microscopic Interpretations**
J. B. BROWN and M. P. FRYER. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **100**, 179–183, Feb., 1955. 5 figs., 10 refs.

The authors review the few reported cases of " self-healing skin carcinoma "—a term suggested by Smith (*Brit. J. Derm. Syph.*, 1934, **46**, 267)—and point out that though many individual lesions regressed, the process as a whole was not arrested in any patient studied for any length of time. They therefore question the validity of the term " self-healing ", and describe one case presenting interesting features. A man of 59 had had multiple squamous-celled carcinoma-like lesions on the arms for 6 years, some of which had regressed spontaneously. The lesions were resected and the sites grafted. On the donor areas on the thighs 18 similar lesions then developed which were considered on clinical grounds to be granulomata, but the histological appearances suggested squamous-celled carcinomata. These lesions regressed and remained healed for 5½ years, during which time 2 further lesions appeared on the arms. The authors do not consider that these lesions were true carcinomata but were the patient's peculiar reaction to trauma or to the dressing. They further consider that the term self-healing carcinoma should not be used until some evidence substantiating it is forthcoming. *Bernard Lennox*

Paediatrics

539. **Bilirubin Encephalopathy. Preliminary Studies Related to Production**
W. J. WATERS and H. A. BRITTON. *Pediatrics* [*Pediatrics*] **15**, 45–48, Jan., 1955. 2 figs., 11 refs.

Staining of the brain can be produced in normal newborn white rats by intraperitoneal injection of a solution of bilirubin. Under similar conditions it was not possible to produce staining of the brain in a comparable series of normal adult rats. This study further emphasizes the importance of the immaturity of the organism in the production of hyperbilirubinemia and its consequent passage through the " blood–brain barrier ". This adds to the increasing evidence that immaturity of biochemical and physiological processes determines the pathological states which appear to be unique to the newly-born organism.—[Authors' summary.]

CLINICAL PAEDIATRICS

540. **Coeliac Disease: Is there a Natural Recovery?**
J. W. GERRARD, C. A. C. ROSS, R. ASTLEY, J. M. FRENCH, and J. M. SMELLIE. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **24**, 23–32, Jan., 1955. 2 figs., 24 refs.

In a study here reported from the University of Birmingham the authors reassessed the condition of 32 patients, 20 girls and 12 boys, who had been diagnosed as suffering from coeliac disease. All had the typical clinical history and none had been treated with a gluten-free diet. It was found that none of the patients was completely free from symptoms, most of them having intermittent diarrhoea with recurrent abdominal pains. They were significantly underweight, below the expected height for age, and skeletal development was retarded in the stunted children. The majority still had steatorrhoea and excreted twice as much faecal fat as control subjects, while the glucose tolerance curve was flat, and radiography of the small intestine with barium still showed the typical abnormal pattern. An iron-deficiency anaemia was present in 19 of the 32 patients. It is concluded that patients treated with a diet which contains wheat gluten do not make a complete recovery.
Winston Turner

541. **" Alimentary " Nitrate Methaemoglobinaemia in Early Infancy.** (Über " alimentäre " Nitrat-Methämoglobinämien im frühen Säuglingsalter)
T. BODÓ. *Monatsschrift für Kinderheilkunde* [*Mschr. Kinderheilk.*] **103**, 8–11, Jan., 1955. 14 refs.

The author reports from the University Paediatric Clinic, Pécs, Hungary, the occurrence of methaemoglobinaemia in 7 infants between the ages of 2 and 10 weeks. All the patients made a good recovery. The presenting clinical picture in these cases was one of restlessness and tachycardia, suggestive of the onset of pneumonia or cardiac failure. The source of the trouble was traced to the use of well-water contaminated with nitrates in making up the infants' feeds. The hypothesis is put forward that the methaemoglobin was formed by nitrate-splitting nitrite-forming bacteria in the duodenum of the infants. Experiments carried out to support this hypothesis are described, in which nitrate solutions were incubated with *Escherichia coli* from the gastro-intestinal tract of very young infants. On simple continuous incubation no change occurred, but with the use of a bouillon suspension and the addition of *E. coli* every 8 hours a high conversion rate of haemoglobin to methaemoglobin was found. The author also contends that the haemoglobin of young babies is easily convertible by contaminated water. *David Morris*

542. **Potassium Metabolism in Gastroenteritis**
B. SCHLESINGER, W. PAYNE, and J. BLACK. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **24**, 33–48, Jan., 1955. 4 figs., bibliography.

Writing from the Hospital for Sick Children, Great Ormond Street, London, the authors discuss potassium metabolism with special reference to the occurrence of abdominal distension and paralytic ileus in infants with gastroenteritis. Hyperkalaemia is often present when the child is dehydrated, and hypokalaemia may develop only when the dehydration is corrected. In a number of cases described it was found that severe abdominal distension, with the consequent risk of ileus, developed as the result of the potassium depletion. The critical level of serum potassium seems to be 12 mg. per 100 ml. (3·1 mEq. per litre). The distension should be treated by continuous gastric and duodenal aspiration, with correction of the dehydration and hypokalaemia. Extra potassium should be given in the intravenous fluids for infusion and later orally only when the initial dehydration has been rectified. The intestinal muscular paralysis appears to result from a cellular potassium deficit and not from the hypokalaemia alone. *Winston Turner*

543. **Acute Distension of the Gall Bladder in Children**
W. RANKIN. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **30**, 60–61, Feb., 1955. 7 refs.

544. **Myocardial Lesions of Early Childhood.** [In English]
E. K. AHVENAINEN and L. HJELT. *Annales paediatriae Fenniae* [*Ann. Paediat. Fenn.*] **1**, 12–26, 1954–55. 6 figs., 14 refs.

At the Children's Clinic, Helsinki, myocardial lesions were detected in 19 out of the total number of necropsies performed between 1946 and 1952 on children dying under the age of 12 months. Of the 19 cases, 14 were found between 1950 and 1952, when 595 necropsies

were performed, an incidence of 2·3%. Inflammatory changes were present in 9 of the cases in this period, an incidence of myocarditis of 1·7%. The cases fell into 4 groups. In the first group of 7 cases there was evident sepsis, the cardiac lesion being a part of more widespread disease; the causal organisms were staphylococci, *Pseudomonas aeruginosa*, and in one case *Candida*. In the second group of 5 cases there were lesions in the myocardium only. One of these patients had a cerebral tumour and another possibly toxoplasmosis; there was one case in this group of Fiedler's isolated myocarditis of unknown aetiology. The third group consisted of 2 cases of foetal endomyocardial fibroelastosis. In the last group of 5 cases myocardial lesions without inflammatory infiltration were found. Two of the patients in this group were twins with kernicterus, independent of the Rh factor; in these some areas of the myocardium were intensely yellow. In another case there were areas of change in the myocardium which stained differently from the remainder of the muscle; this patient had had severe anoxia.

The authors state that myocarditis in childhood does not appear to be common and is difficult to recognize clinically; they suggest that it would be diagnosed more frequently if electrocardiography were carried out systematically in diseases of early childhood. Primary myocarditis is rare and its aetiology obscure.

E. H. Johnson

545. **Interstitial Plasma Cell Pneumonia**
J. H. LUNSETH, T. W. KIRMSE, A. P. PREZYNA, and R. E. GERTH. *Journal of Pediatrics* [*J. Pediat.*] **46**, 137–145, Feb., 1955. 5 figs., 12 refs.

A presentation has been made of what we consider to be the first instance of interstitial plasma cell pneumonitis reported from the United States. The clinical features of this case and of the disease in general are presented and discussed. The pathologic changes are discussed. The occurrence of abundant smooth muscle in the walls of the alveolar ducts is stressed, and it is suggested that this may in part explain the final pulmonary failure. The clinical and pathologic resemblance between interstitial plasma cell pneumonitis and the Hamman–Rich syndrome is noted.—[Authors' summary.]

546. **Staphylococcal Pulmonary Infection in Infancy**
D. MAGNER and N. KUSSNER. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **24**, 1391–1401, Dec., 1954. 8 figs., 18 refs.

The clinical picture and the pathological findings in 9 cases of staphylococcal pneumonia in infancy seen over a period of 11 months at the General Hospital, Ottawa, are discussed. The authors emphasize the fulminating character of the illness, which in some cases lasted only a few hours. A right-sided acute otitis media preceded signs of pulmonary infection in one case, this being the only one in the series in which there was a focus of staphylococcal infection elsewhere than in the lungs. The authors consider that in the remainder the route of infection was bronchogenic and the source environmental. In all cases multiple lung abscesses were found at necropsy and it is suggested that these developed from small areas of necrotizing pneumonia, which, when situated near the pleura, gave rise to the empyema which was present in all 9 cases and is regarded by most workers as an integral part of the disease. *J. B. Wilson*

547. **Variation of the Blood Bromide Level with Age in Healthy Children.** (О возрастных колебаниях содержания брома в крови здоровых детей)
Y. B. VISHNEVSKII and L. A. KABRANOVA. *Педиатрия* [*Pediatrija*] 54–59, No. 1, Jan.–Feb., 1955. 3 figs.

It has been reported by Kryuchkov and Ostrovskaya that in children with a high blood bromide level the processes of excitation and inhibition in the central nervous system are well balanced, while those with a low blood bromide content tend to suffer from restlessness, anorexia, and loss of weight. At the Leningrad Academy of Medical Sciences the blood bromide level was determined in 111 healthy children aged 11 days to 15 years and in a control group of 25 young adults. The following results were obtained (the age groups containing approximately equal numbers of subjects).

Age	Average Blood Bromide Concentration
0–1 year	11·02 mg. per 100 ml.
1–3 years	8·48 ,, ,,
3–7 ,, ...	6·25 ,, ,,
7–13 ,, ...	7·63 ,, ,,
13–15 ,, ...	6·24 ,, ,,
Young adults ..	6·27 ,, ,,

The high blood bromide value found in the youngest group is related to the relatively inactive cerebral cortex and sluggish nervous processes at that age, while the rise in the value at 7 to 13 years is related to the development of maximum inhibitory regulating control of the cortex. Finally, it is noted that the lowest value is found at the time of adolescent hormonal imbalance.

In a second study 40 children were observed and classified as " excitable ", " inhibited ", and " level-headed ", and their blood bromide level was then determined. No clear correlation between the two was found. During a first attack of acute rheumatism in a boy of 11 years the blood bromide level was found to vary with the stages of the illness. *Edward D. Fox*

548. **The Role of Cerebral Phlebitis in Acute " Encephalitis " in Childhood.** (Le rôle des phlébites cérébrales dans les " enoéphalites " aiguës de l'enfant)
M. BERNHEIM, P. F. GIRARD, and F. LARBRE. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **31**, 255–268, Jan. 20, 1955. 12 figs., 5 refs.

The clinical and pathological aspects of cerebral venous thrombosis in infancy are discussed at some length, with special reference to 8 cases observed at the Hôpital Edouard-Herriot, Lyons, and to the French literature on the subject. Some excellent illustrations of post-mortem material are incorporated. The most noteworthy feature of the study is the authors' contention that heparin is a useful agent in the treatment of this condition.

M. E. MacGregor

549. **Thrombosis of Deep Veins in Childhood. I. Thrombosis of the Dural Venous Sinuses.** [In English]
E. K. AHVENAINEN and N. HALLMAN. *Annales paediatriae Fenniae* [*Ann. Paediat. Fenn.*] **1**, 3–11, 1954–55. 1 fig., 8 refs.

Out of 1,958 cases on which necropsy was performed between 1947 and 1952 at the Children's Clinic, University of Helsinki, thrombosis of the deep veins was found in 15. In 11 of these the thrombus was located in an intracranial sinus—an incidence of 0·56%. In each of the 11 evidence of infection was present at necropsy: intestinal infection only (3 cases), pneumonia (4), enteritis with mastoiditis (1), *Salmonella* meningitis (1), interstitial plasma-cell pneumonia (1), and tuberculous meningitis (1). In all except one case the sagittal sinus was involved; the ventricles of the brain were distended only in patients with meningitis. There were no clinical signs pointing to sinus thrombosis.

In 1949 sinus thrombosis was found at necropsy in 3 out of 50 cases of gastroenteritis. The infants had been ill for more than 10 days and in all 3 there was a second rapid dehydration with profuse vomiting. Acidosis was not particularly marked. The thrombosis appeared to be associated with an abrupt loss of weight, but anaemia did not play any important part, and examination of the cerebrospinal fluid did not reveal any definite changes.

E. H. Johnson

550. **A Study on Boric Acid Absorption in Infants from the Use of Baby Powders**
D. E. JOHNSTONE, N. BASILA, and J. GLASER. *Journal of Pediatrics* [*J. Pediat.*] **46**, 160–167, Feb., 1955. 19 refs.

An investigation was carried out at the Genesee and Strong Memorial Hospitals (University of Rochester School of Medicine), Rochester, New York, into the possibility that the use of a proprietary dusting powder containing 5% of boric acid may give rise to boric acid poisoning in babies. Eight mentally retarded children with healthy skin having been selected for investigation, weekly samples of their blood and urine were examined and the boron content determined colorimetrically, first during a control period of 6 weeks during which powder containing no boric acid was used, and then for another 6 weeks during which the powder under test was freely applied to the napkin area at each change. Another infant, who had second-degree burns of the napkin area, was also studied, 5 to 10 g. of the powder being sprinkled over the burned area 4 times daily for 3 days.

The average blood boron concentration during the control period varied from *nil* to 0·9 part per million [1 p.p.m.=0·1 mg. per 100 ml.] with the exception of one reading of 7·8 p.p.m. [in a child whose blood boron content is not given for the remainder of the control period]. During the period that dusting powder containing boric acid was in use the average boron content of the blood varied from *nil* to 1·1 p.p.m., except for isolated readings of 2·3, 5·2, and 9·3 p.p.m., all in different children. These details are given in tables together with statistical analyses [of doubtful value in so small an experiment]. The boron concentration in the blood of the burned child was 0·2 p.p.m. before application of the powder and rose no higher than 0·6 p.p.m. during its application.

It is claimed that all the fatal cases of boric acid poisoning reported in the literature have originated from the use of high concentrations of boric acid in powder or solution, and that only one doubtful case of poisoning at all has arisen from the use of powders containing 5% or less of the acid The accuracy of the commonly used turmeric-paper test for the determination of boron in blood and urine is questioned and current lack of knowledge concerning the lethal concentration of boron in the blood and tissues is emphasized, a figure of 500 to 2,500 p.p.m. obtained "from autopsy material" being preferred by the authors to the "absurdly low" figure of 50 p.p.m. given by other authorities. It is pointed out that boric acid is added to talcum in commercial dusting powders primarily as a buffering agent rather than as an antiseptic, because talcum contains a small quantity of calcium oxide and other alkaline salts. Thus when the dusting powder is wetted, borates are formed which are not absorbable through the skin.

[The authors' summary is not understood; it states that "the highest value for blood boron concentration did not exceed 0·6 parts per million", which was true only of the burned child.] *M. A. Dobbin Crawford*

551. **Boron Absorption from Borated Talc**
R. S. FISHER, H. C. FRIEMUTH, K. A. O'CONNOR, and V. JOHNS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 503–505, Feb. 5, 1955. 11 refs.

The absorption of boron from skin dusted with talc containing 5% of boric acid was studied in 60 mentally retarded infants and young children over a period of one year. The powder was applied freely to the napkin area after each change, and elsewhere to the skin as needed, the average quantity used per infant being 168 g. per month.

Blood samples were taken from every child in the ward before the start of the study to obtain a base value and thereafter every two months. The boric acid content of the blood was determined colorimetrically. (Details of the procedure are yet to be published.)

The blood boron level of these infants before the application of the dusting powder was 0·005 mg. per 100 ml., which is lower than in infants living at home, in whom it frequently reaches 1 mg. per 100 ml. During the year of the trial the average blood boron content varied from *nil* to 0·075 mg. per 100 ml., the over-all average being 0·0125 mg. per 100 ml.—an insignificant increase. The individual concentrations were, however, erratic, the lowest being observed during a period of hot weather when the children had miliaria of mild to moderate severity.

It is stated that "careful review of the world literature does not show a single authenticated case of boric acid poisoning due to the use of borated talc". The relatively high boron content of fruits and other articles of diet is discussed, and it is emphasized that there is no evidence that boric acid is a cumulative poison. The unreliability of the turmeric test for boron in urine is stressed. *M. A. Dobbin Crawford*

Medical Genetics

552. **The Investigation of a Large Family Affected with von Willebrand's Disease**
J. C. W. MACFARLANE and M. J. SIMPKISS. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **29**, 483–487, Dec., 1954. 1 fig., 21 refs.

In this communication from the Hospital for Sick Children, Great Ormond Street, London, the literature on the hereditary haemorrhagic diathesis known as von Willebrand's disease is extensively reviewed and a large family in which many affected individuals have occurred is described. Among 64 members of the family for whom information was available, 21 belonging to five generations were affected. A genealogical tree of this family is given.

In 11 affected individuals who were studied in detail clot retraction was normal, there was no defect of the blood coagulation factors, and no abnormality of the number, morphology, or function of the platelets. Thrombin generation, thromboplastin generation, and prothrombin consumption tests showed no abnormality, nor was there any quantitative or qualitative defect of fibrinogen. The only pathological finding was a prolongation of the bleeding time during a bleeding phase and some suggestion of abnormalities in the nail-bed capillaries.

The pattern of bleeding was remarkably uniform. Of the 21 affected members, 16 had recurrent epistaxis as the main symptom, 11 suffered from prolonged bleeding following dental extraction, and 7 bruised rather easily. No case of haemarthrosis, haematuria, or haemorrhage into any cavity or organ was encountered. The haemorrhagic tendency appeared to be cyclic and to decrease with age.

The authors suggest that any surgical operation required could safely be performed—as was done in one of these patients—during the phase when the bleeding time is normal. The condition can be attributed to a single dominant gene, the affected individuals being heterozygous for this. *H. Harris*

553. **The Hereditability and Pathogenetic Significance of Pectus Excavatum.** (Ereditarietà e significato patogenetico del " pectus excavatum ")
S. BATTAGLIA and T. MASINI. *Folia hereditaria et pathologica* [*Folia hered. path.* (*Pavia*)] **4**, 73–110, Feb., 1955. 10 figs., bibliography.

The authors report 7 cases of pectus excavatum (funnel chest) studied at the University of Pavia. In 2 instances no other member of the family was affected in the same way, while one patient's mother was so affected, the father, a sibling, and a first cousin of another were affected, two patients—identical twins, both affected—had an affected uncle and step-sibling, and a brother and the maternal uncle of the last patient were affected. A number of other anomalies, including deaf-mutism, congenital goitre, micrognathia, macroglossia, and absence of the soft palate, were found in the index cases, while similar malformations, including congenital dislocation of the hip, deaf-mutism, hare-lip, and micrognathia, were found among the relatives of the index cases.

It is noted that a dominant gene of varying manifestation would explain the occurrence of pectus excavatum in these families and those previously reported, though it is not clear whether the other malformations not uncommonly found in association with funnel chest are expressions of the same gene. The sex incidence varies in different series, but most authors agree that the ratio of males to females is at least 2 to 1.

A comprehensive table of the familial instances of funnel chest which have previously been reported is appended to the paper. *C. O. Carter*

554. **Hereditary Vascular Tumors of the Nervous System**
M. L. SILVER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 1053–1056, Nov. 13, 1954. 1 fig., 9 refs.

The hereditary tendency in haemangiomata of the nervous system (Lindau's disease) has been noted by a number of workers, and in the present paper a single family is described in which these tumours occurred through several generations. Adequate information was available concerning 61 individuals in the family; in 19 of these there was clinical verification of the presence of vascular tumours and in 8 there were symptoms presumptive of these lesions. The proved cases were distributed over six generations of the family, and study of the family tree suggested that the condition was inherited as a Mendelian dominant (or heterozygous) trait. Considerable variation was observed in the extent of the lesions and the age at onset of clinical symptoms.
H. Harris

555. **Familial Hydronephrosis**
R. B. RAFFLE. *British Medical Journal* [*Brit. med. J.*] **1**, 580–582, March 5, 1955. 1 fig., 6 refs.

556. **Familial Occurrence of Juvenile Diabetes Mellitus Associated with Diabetes Insipidus.** (Sul diabete giovanile misto famigliare)
D. CASA. *Acta geneticae medicae et Gemellologiae* [*Acta Genet. med.* (*Roma*)] **4**, 230–241, May, 1955. 7 figs., bibliography.

557. **A Contribution to the Genetics of Madelung's Deformity.** (Contributo alla genetica della deformità di Madelung)
I. GATTO. *Acta geneticae medicae et Gemellologiae* [*Acta Genet. med.* (*Roma*)] **4**, 205–216, May, 1955. 10 figs., 11 refs.

Public Health

558. **Socioeconomic Distribution of Cancer of the Female Sex Organs in New Haven**
E. M. COHART. *Cancer* [*Cancer (N.Y.)*] **8**, 34–41, Jan.–Feb., 1955. 6 figs., 4 refs.

Details of the cases of cancer of the breast, ovary, and uterus which occurred among women in New Haven, Connecticut, between 1935 and 1949 were collected from the records of the Cancer Morbidity Register of the State Health Department and from death certificates. These cases were distributed among the 24 ecological districts into which the town had been divided for sociological purposes. An estimate of the sex and age distribution of the population of each district was made from special census reports, and the expected number of cases of cancer of these organs calculated from the age-specific incidence rates for the whole town. The districts were then grouped to make 7 socio-economic areas, which in turn were grouped in 3 regions occupied broadly by the rich, the middle class, and the poor.

As in other investigations, the incidence of cancer of the breast and ovary was found to increase progressively from the poorer to the wealthier areas. The differences were statistically significant for cancer of the breast, but not for ovarian cancer. In contrast to other investigations, however, no consistent differences were found between the observed and expected incidence of cancer of the uterus. Socio-economic status was correlated with the stage of the disease on admission to hospital in cancer of the breast, and the 5-year survival rate for breast cancer was correspondingly higher for women in the more well-to-do categories. The proportion of married women was significantly higher among women with cancer of the cervix than among women with cancer of the breast, ovary, or fundus uteri. *Richard Doll*

559. **The Development of the Domestic Help Service**
C. GRANT. *Royal Sanitary Institute Journal* [*Roy. sanit. Inst. J.*] **75**, 235–243, March, 1955.

Under the National Health Service Act, 1948, local authorities in England and Wales were empowered to provide domestic help in cases of need, and in this paper from the Department of Health for Essex, Chelmsford, the number of cases in the county in which such help was given and the hours of service are analysed. A table gives details of the maternity cases, acute and chronic sick, aged sick, aged non-sick, tuberculous cases, and miscellaneous cases in which domestic help was given in the years 1950 to 1953 inclusive. The figures are not related to population or to potential needs.

The table shows that in all groups except the chronic sick there was a fall during the period under review in the number of cases receiving help and, so far as the figures show, in the number of hours of service. [Case averages are not given but this is commented on below.] This fall was not due to any diminution in sickness or increase in institutional treatment, and the author suggests that it is " natural during the settling down process of a new service ". By contrast, the number of chronic sick helped each year increased (by 1953 it had more than doubled), though the hours of service given again showed a reduction.

The significance of some of the figures is discussed and proposals are made for future developments, special emphasis being placed on the need for more workers and for a short training course and the desirability of providing meals and laundry service. The case for establishing a night attendance service is argued and the author questions whether this should not more properly be provided by the home nursing service. It is concluded that " by training helps . . . a ' care ' service could become an integral part of the preventive services ".

[The figures are valuable so far as they go, but more detail and analysis would have increased their significance. Rough calculations appear to show that the service given to each case varied from 80 hours in maternity cases in 1950 (falling to 60 in 1953) to nearly 300 in 1950 in cases of tuberculosis (falling to about 246 in 1953). The average for all cases works out at some 150 hours a year, or less than half an hour daily. If this includes shopping and cooking for the increasing numbers of aged and chronic sick who form the majority, some of the staff must be working at flash-point.]

R. J. Matthews

560. **The Survival of Dysentery Bacilli in Boiled Tap Water.** (О выживаемости дизентерийных бактерий в кипяченой воде)
V. P. KRŸLOVA. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] No. 2, 68–70, Feb., 1955.

The object of this investigation was to determine whether the general assumption that the bacilli of dysentery survive for only a short period in boiled tap water has any foundation in fact, particularly as one of the principal prophylactic recommendations with regard to gastro-intestinal infections is to boil all drinking water. It is noted that even boiled water, if kept in open bottles or jugs for any length of time, would be subject to secondary infection. In all, 10 experiments were carried out with *Shigella sonnei*, *Sh. paradysenteriae* (Flexner), and *Sh. dysenteriae* for their capacity to survive in boiled tap water, and for comparison 4 experiments with *Salmonella typhosa*. The boiled water was distributed in amounts of 250 ml., inoculated with either 10,000 or 100 micro-organisms per ml., kept at room temperature, and cultured at intervals by direct inoculation on to " endo " agar plates. The cultures isolated were fully investigated in the usual way.

In the water contaminated with the larger dose of organisms *Sh. sonnei* was isolated for 45 to 100 days, the Flexner strain for 11 to 56 days, and *Sh. dysenteriae* for 14 to 15 days after infection; in comparison,

S. typhosa survived for 17 to 22 days. In the samples contaminated with 100 organisms per ml. the corresponding figures were 38 to 94 days, 7 to 50 days, and 3 to 5 days respectively, and for *S. typhosa* 7 to 10 days. The author emphasizes that the unexpectedly long survival time of dysentery bacilli in boiled tap water must be taken into account in all future prophylactic measures against gastro-intestinal infections.

[It would have been very helpful in assessing these results if the author had provided some data on the content of organic material (if any) of these water samples before they were contaminated in the way described.]

K. Zinnemann

EPIDEMIOLOGY AND IMMUNIZATION

561. **Observations on the Efficacy of Reimmunization against Diphtheria by Means of a Toxoid Plaster.** (Osservazioni sull'efficacia della vaccinazione antidifterica di richiamo mediante il cerotto all'anatosina)
A. Rosa, M. La Placa, A. Fusaroli, and G. Lodi. *Clinica pediatrica* [*Clin. pediat.* (*Bologna*)] **36**, 727–745, Oct., 1954. 1 fig., 30 refs.

The authors, writing from the University of Bologna, point out that owing to the low incidence of diphtheritic infection in the population at large there exists a highly susceptible adult population with a diminished opportunity of acquiring natural immunity by subclinical infection. As immunization against diphtheria is not enforceable by law, a simple and painless method of immunization would have obvious appeal to the epidemiologist. They have therefore experimented with a method devised by D'Antona in which the toxoid is applied to the skin by means of a plaster. The authors consider that Schick-test negativity is not an absolute indication of immunity to diphtheria and they prefer to use a neutralization technique in rabbits to determine the actual titre of antibody.

In a first series of 100 children aged between 4 and 12 years of age, all of whom had been immunized 1 to 10 years previously, a plaster containing 100 units of toxoid was applied to the prepared skin in the subclavicular region and left in position for 72 hours; blood samples were taken before its application and 23 days afterwards. The results, which are tabulated, showed that an increase in antitoxin titre occurred in all children, but only 38% of those susceptible beforehand (less than 0·01 units of antitoxin per ml. of serum) became immune. In order to evaluate the naturally acquired immunity of a child population over a period of observation, another group of children were given a booster dose of toxoid by the plaster technique and compared with a group of untreated children living in the same institution; 33% of susceptible treated children became immune, but in none of the controls was there spontaneous conversion during the period of observation.

The results in these two series were statistically evaluated, and the authors conclude that, compared with a 95% conversion rate by injection of much smaller amounts of toxoid, the results obtained by the present method are much less satisfactory; a second application of the toxoid plaster in another series, however, brought the conversion rate up to 53% of susceptible subjects. This, while admittedly not good enough, is felt to justify further exploration of the possibilities of the method.

F. Hillman

562. **The Duration of Immunity following Antidiphtheritic Immunization with Toxoid.** (Sulla durata della immunità conseguente alla anatossivaccinazione antidifterica)
A. Rosa, R. Olivo, and M. La Placa. *Clinica pediatrica* [*Clin. pediat.* (*Bologna*)] **36**, 746–761, Oct., 1954. 1 fig., 25 refs.

The authors believe that the great variation between the different results reported in the literature regarding the duration of the immunity conferred by antidiphtheritic immunization depends on the type of toxoid used, the number and route of, and interval between, immunization doses, and most of all on the environment, that is, the carrier rate in the particular population. In their opinion the duration of immunity will decrease with the increasingly widespread use of artificial immunization.

In a study carried out at the University of Bologna they determined the level of the circulating antitoxin titre in 287 children who had been immunized from less than one to more than 7 years previously, the technique used being Jensen's toxin–antitoxin neutralization technique carried out in rabbits. Taking an antitoxin titre of more than 0·01 unit per ml. of serum as indication of immunity, the highest percentage (80%) of immune children was found among those who had been immunized 1 to 3 years previously; at 4 years after previous immunization the figure was only 40%, but at 5 to 7 years it increased again, probably owing, it is thought, to a build-up of natural immunity. Of the children immunized less than one year previously, only 36% had a circulating antitoxin titre of more than 0·01 unit per ml. of serum.

Interpreted in relation to the age of the children, these results suggest that immunization is effective from 2 to 5 and by the time they are 10 they will have acquired natural immunity. Since those between the ages of 5 and 9 are the most susceptible, it is suggested that a booster dose given 3 years after the primary immunization is desirable.

F. Hillman

563. **Crowds and Poliomyelitis: with Special Reference to a Recent Epidemic in Western Australia**
D. J. R. Snow. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 2–5, Jan. 1, 1955. 3 figs.

The influence of crowds on the spread of poliomyelitis is discussed in this paper, with reference to the conditions prevailing at the time of the Royal visit to Western Australia in March, 1954, when large crowds assembled repeatedly over a period of 6 days during a severe epidemic of poliomyelitis. No special measures were taken to control the size and distribution of the adult groups, and relatively few country people stayed away from the metropolitan areas because of the epidemic. Thousands assembled at each function and there

must have been close contact between susceptible and potentially infectious subjects. The weekly notifications of poliomyelitis reached a peak almost immediately before the Royal visit, and the downward trend appeared to be uninfluenced by the mass gatherings. Admittedly, special precautions were taken to assemble children in their own school groups under strict supervision, and there was virtually no contact between the various groups. In one instance, moreover, a review of some 60,000 children was cancelled.

The general control measures included isolation for 14 days of patients suffering from poliomyelitis and "house-and-garden" quarantine for close contacts under 15 years of age. Certain adult contacts—for example, teachers and food-handlers—were excluded from work. Wide publicity was given to the importance of hand cleanliness and to the harmful effects of fatigue. Early symptoms of the disease were made known to the public, and immunizing injections, dental operations, operations on the nose and throat, and swimming classes were suspended. A campaign against flies was instituted. The control measures laid more stress on hand hygiene than on the prevention of droplet infection, and it is suggested that the absence of any conspicuous increase in notifications was consistent with the intestinal–oral method of spread. *A. Garland*

564. The Human Source of Tuberculous Infection in Children

B. Briggs, R. S. Illingworth, and J. Lorber. *Lancet* [*Lancet*] **1**, 263–266, Feb. 5, 1955. 3 refs.

While the mortality from tuberculosis in childhood has fallen rapidly in recent years, there has not been a corresponding fall in morbidity from this disease, and for this reason the authors have studied the history, especially the history of contact, of 564 children with active intrathoracic or generalized tuberculosis who were treated in the wards or as out-patients at the Children's Hospital, Sheffield, between January, 1947, and December, 1952. In 163 cases the information obtained was incomplete, and the main results and conclusions are based on the remaining 401 patients. Of these, 73 (18%) were under 1 year of age and 101 (25%) between 1 and 2 years, and 181 were admitted for miliary or meningeal tuberculosis. The investigation was conducted with the help of chest physicians and included, where necessary, re-examination of contacts.

A human source of infection was found in 70 (96%) of the infants under 1 year of age, 86% of children between 1 and 2, 85% of those between 2 and 4, and 64% of those aged 5 to 14. The father had tuberculosis in 119 cases, the mother in 108, other relations in 143, and unrelated contacts in 46. Contact within the household was noted in over three-quarters of the cases. Bovine sources of infection were not followed up. In about 10% of the cases the source of infection was not known before the investigation. In many others the usual precautions had not been taken, and the authors, as a result of a detailed inquiry into this aspect of the problem, found that common faults were delay in *x*-ray examination and re-examination of the infecting case; failure to notify; inadequate follow-up, especially of supposed sputum-negative cases; inadequate instruction of infectious subjects; a casual attitude to the dangers of contact at home, at clinics, and in the homes of neighbours (children assembling around the television set of an infectious patient is especially mentioned); and incomplete segregation of infants, even when receiving B.C.G. vaccine, from infectious adults.

[This paper is highly interesting and raises the whole question of responsibility towards contacts. The recent emphasis on the clinical or consultant status of the tuberculosis physician, though justifiable, seems to have left gaps in the chain of public health control. While the authors discuss the differing responsibilities of those concerned, including health visitors and general practitioners, it seems to the abstracter that the outstanding conclusion to be drawn from this paper is that integration under one head of all forces concerned with home supervision and the follow-up of infectious subjects and their contacts is essential. Many of the cases in the present series could have been prevented.] *R. J. Matthews*

565. The Control of Tuberculosis. House to House Spread of Disease

R. Greenville-Mathers, H. J. Trenchard, and D. J. Wheeler. *Tubercle* [*Tubercle* (*Lond.*)] **35**, 294–301, Dec., 1954. 3 figs., 4 refs.

To determine whether the present method and rate of rehousing tuberculous subjects is a source of danger to other households, the authors, at the Harrow and Edgware Chest Clinics, Middlesex, compared the incidence and geographical relationship of tuberculous households in a housing estate completed in 1930 (Estate A, of 4,173 houses and a population of 16,000) with that in an old housing area (Estate B, of 5,067 houses and a population of about 20,000), the families in both estates being of the same social and economic status. The two estates were approximately equal in area, and for most of the period of investigation—1930 to 1951—both were in the charge of the same tuberculosis physician with full radiological and bacteriological facilities. The age and sex distribution of the two populations differed somewhat, but with estates established at different times this was inevitable.

During the 20 years under review there were 505 new tuberculous households in Estate A, the notification being "primary" for 395 and "transfer in" for the remainder. In Estate B the number of new tuberculous households was 413, notification being "primary" for 357. Maps and tables give details of the survey, which included careful consideration of the approximation of dwellings, "block" arrangements and common entries, the spatial pattern of affected houses, and the household-years at risk. For these the text must be consulted, but the authors conclude [reasonably enough on the evidence] that the present method and rate of rehousing tuberculous subjects in the area has not brought about any appreciable risk of spread of the disease. The findings are compared with those of a similar investigation carried out in Northampton, and reasons for the differences in results are discussed. *R. J. Matthews*

Industrial Medicine

566. **Sickness in a Health Department of a Local Authority**

R. T. Bevan and E. Lewis-Faning. *Monthly Bulletin of the Ministry of Health and Public Health Laboratory Service* [*Monthly Bull. Minist. Hlth (Lond.)*] **13**, 178–193, Oct., 1954. 3 refs.

The authors have studied absence due to sickness among 975 full-time members of the staff (all categories) of the Health Department of the Glamorgan County Council during the 52 weeks commencing April 1, 1951. The total possible working days in the year is taken as 312 days (52 weeks of 6 days) per person; there were 82 new entrants during the year and 98 employees left, giving a total number of possible working days for the whole department of 274,062, of which 13,320, or 4·86%, were lost through illness. Analysis of the sickness rates according to age, sex, and (for women) civil status showed that the average number of days lost per capitem per annum among the 795 employed for the whole year varied from 2·0 (in males aged 15 to 20) to 68·4 (in widowed females aged 55 to 60), the average figures for all males being 6·4, for single females 11·2, for married females 20·6, and for widows 44·1. In general, as would be expected, the average duration of illnesses experienced increased with age, especially in women.

The figures for new entrants and for those leaving the service during the year differed markedly from the above, 15% of possible working days being lost in the latter case. There were marked differences also between different types of employee. Among the males the sickness rate for administrative staff was higher than for ambulance staff, while among the females home helps and home nurses showed sickness rates above the average. The rate for home helps was far greater than for any other type of employee and was double that expected from the rate for all groups. The reasons for these differences are discussed, and age, lack of training, and lack of incentive are suggested as contributory causes of the high sickness rate among home helps and of the relative instability of this service (only 61% of home helps being employed for the whole year).

The categories of sickness responsible for the greatest proportion of time lost were diseases of the upper respiratory system (chiefly common cold) and of the locomotor system (chiefly rheumatism), which together with other respiratory diseases accounted for over 40%. Diseases of the digestive system accounted for about 12% of the total days lost, while allergic, endocrine, metabolic, nutritional, and circulatory diseases (grouped together) come next in order (6·75%). A high incidence of digestive illness among ambulance workers is noted. Sickness of less than 3 days' duration (not requiring a medical certificate) accounted for 63% of the total number of "incidents" among female administrative workers, whereas for home nurses and midwives only 14% and 9% were of this nature. On the other hand, 22% of the illnesses of home nurses and 17% of those of midwives were of more than 6 weeks' duration as against only 1% of those of female administrative workers.

[This paper is illuminating and contains many data which should prove valuable for comparison with other work on the same lines. The denominator of 312 days for the potential working year is, in the abstracter's opinion, too high and results in the picture being presented in a somewhat rosier light than that of reality. Even so, some of the figures are rather startling for occupations which in many cases are relatively sedentary.]

R. J. Matthews

567. **Psychiatric Disability and Employment. I. A Survey of 222 Registered Disabled Persons. II. A Follow-up of 95 Unemployed Subjects**

M. Markowe, W. L. Tonge, and L. E. D. Barber. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] **9**, 39–45 and 46–47, Jan., 1955. 14 refs.

Two groups of subjects registered under the Disabled Persons (Employment) Act, 1944, as suffering from psychiatric disability were studied by the Medical Research Council Unit for Research in Occupational Adaptation. One group had been unemployed for at least 6 months during the years 1950–3, while the other group had had less than 3 months' unemployment during the same period. There were 95 subjects (average age 41·65 years) in the unemployed group, and 127 (average age 42·43) in the employed group, the latter constituting those (22%) of a much larger group approached who attended for interview. After an hour's interview by a psychiatrist the mental health of each subject was assessed on a five-point scale, and various tests and other sources of information were used.

Among 120 subjects with affective disorders or hysterical and obsessional states, 105 had had more than 3 years' illness, and in this group there was a clear association between severe mental ill health and unemployment. The majority of the 15 schizophrenics were unemployed, and there was also a majority of unemployed among the 35 subjects judged psychopathic (inadequate personality or gross emotional instability) at the interview. The 14 unemployed mental defectives were all older than the 10 who were employed, and also had a lower level of general intelligence as shown by the "dominoes" test. There was a higher proportion of unmarried men among the unemployed. Comparison of the modal income of unemployed men with the income previously earned showed that married men without dependants had the highest financial incentive to return to work. Moreover, the employed men tended to earn higher wages than the unemployed had received when last at work. Although it appeared that "unemployment and mental ill-health have an effect of mutual enhancement", there was no evidence that the unemployed men were, as a group, more severely ill than the employed. The authors conclude that the

occupational adaptation of psychiatrically disabled subjects is chiefly governed by quality of personality, and that their successful rehabilitation depends largely on whether the previous history shows a stable personality and a satisfactory work record.

In the second part of this investigation the work records of the 95 unemployed subjects studied were followed up over a period of 12 months. While the highest average number of weeks of work was achieved during that period by those with neurosis of recent onset, the work record of all groups except the mental defectives and those suffering from involutional conditions showed an improvement over that for the previous year.

The 25 subjects who voluntarily attended a special clinic set up to deal with the problems of the psychiatrically disabled were generally older and more ill than the other subjects. In comparison with a control group equivalent in age, diagnosis, and mental health who did not attend, they did not show any greater improvement in work record despite the help received, usually in the form of social services, while some showed a deterioration in mental health. It is concluded that " sickness is a greater deterrent to employment in those who are marginally employed than in those with good work records, and that measures more vigorous than outpatient treatment are needed to secure their rehabilitation ". *J. F. Mackworth*

568. **Standards of Fitness among Drivers of Commercial Vehicles. A Socio-medical Investigation Based on Wartime Records of Civilian Medical Boards**
J Webb. *British Medical Journal* [*Brit. med. J.*] **1**, 515–517, Feb. 26, 1955. 4 refs.

Although the statutory licensing authorities require applicants for licences to drive public service vehicles to pass a medical examination, with tests of vision, no such medical test is required of drivers of commercial vehicles. The investigation here reported was therefore carried out to assess the general level of fitness of professional drivers of road vehicles through the medium of the records of examinations carried out by civilian medical boards on 1,276 such drivers between 1941 and 1944. These were from three areas, 577 being from Essex, 273 from Leicester, and 426 from Northampton, while 761 were described as lorry drivers, 406 as drivers of vans and other commercial vehicles, 31 as drivers of public service vehicles, and 78 as of such occupations as chauffeurs, drivers of ambulances, and road patrols. Of these 1,276 drivers, 99 were placed in Grade 4, that is, not fit for any form of military service, and 83 in Grade 3, that is, fit for light duties only, these also being in practice rejected for military service.

There were 3 men whose visual acuity was 6/60 : 6/60 and who had no spectacles, 4 whose visual acuity was 6/60 : 6/36 after correction, and 4 whose good eye could not be improved beyond 6/24. In all, 49 (3·8%) of the drivers fell below the visual standard which is required for a licence to drive a public service vehicle, and 178 (14%) below the somewhat higher standard which is required by the London Transport Executive for their bus drivers.

Of 5,541 pedestrians and pedal cyclists killed in road accidents during the years 1948 and 1949, 2,039 were knocked down by goods transport vehicles, 869 by buses or trams, and 158 by coaches or taxis. Thus in more than half of the accidents causing the death of a pedestrian or pedal cyclist the mechanically propelled vehicle was in charge of a professional driver. *K. M. A. Perry*

569. **Vinyl Carbazole as a Hazard to the Skin in the Chemical and Electrical Engineering Industries.** (Vinylkarbazol als hautschädigende Noxe in der chemischen und elektrotechnischen Industrie)
W. Gockell. *Berufsdermatosen* [*Berufsdermatosen*] **3**, 9–14, Jan., 1955. 4 refs.

Vinyl carbazole is not a primary toxic material but is a powerful sensitizing agent. The colourless crystals melt on heating at 65° to 67° C. and boil at 110° C. Pure vinyl carbazole, kept in the cold, is lastingly stable, and is stable also in the presence of alkalis, but a small proportion of acid will suffice to induce decomposition to carbazole and acetaldehyde. Under the influence of heat or short-wave light it turns yellow and polymerizes; the polymerized material has very slight sensitizing properties. Vinyl carbazole is used mainly as an insulator for electrical components and for the impregnation of materials which may be required to resist heat, water, and corrosion.

In this paper from the Municipal Hospital, Ludwigshafen, after a short review of the literature the author presents detailed clinical histories of 2 cases of severe generalized sensitization dermatitis which resulted from industrial contact with vinyl carbazole. The patients showed an erythematous eruption, with marked oedema, eroded weeping patches, and haemorrhagic areas, involving the entire body except for the palms of the hands and the soles of the feet. In the first case there was a moderate stomatitis and the oedema extended to the nasal mucosa, interfering with breathing; the skin condition was accompanied by a rise of temperature to 39° C. (102° F.), an eosinophilia (10%) was present, and there were toxic granules in the cells of the blood. In the second case the mucous membranes were not involved, but the temperature rose to 40° C. (104° F.), the eosinophil granulocytes made up 24% of the total leucocyte count, and there were signs of damage to the myocardium and to the liver parenchyma.

Both workmen recovered quickly and completely on removal from contact with the noxious agent and after treatment with antipyretics, vitamins, and antihistamines, penicillin being given in the second case only. The skin was treated with wet compresses and with a zinc dusting powder. It is interesting to note that a recurrence was experienced by the second man after using his former tools at work in a place remote from the shop where vinyl carbazole was in use. The results of patch tests, which are fully described, indicate the potency of vinyl carbazole. Cyclohexane was the solvent in use, but patch-testing with pure cyclohexane gave a negative result; however, a solution of vinyl carbazole in cyclohexane in a concentration of only 1 in 1,000,000 gave a positive result. *M. A. Dobbin Crawford*

Forensic Medicine and Toxicology

570. **The Liver in Ferrous Sulfate Poisoning. A Report of Three Fatal Cases in Children and an Experimental Study**
M. A. LUONGO and S. S. BJORNSON. *New England Journal of Medicine* [*New Engl. J. Med.*] **251**, 995–999, Dec. 16, 1954. 1 fig., 12 refs.

Since 1947 many cases of poisoning following accidental ingestion of ferrous sulphate tablets have been reported, most of them in children who have been attracted by the bright colour and sweet taste of the tablets. In this paper from Harvard Medical School, Boston, the authors discuss the various views on the nature of the hepatic damage in fatal cases in these children, and describe 3 cases of their own. They also describe an experimental investigation of ferrous sulphate poisoning in animals. Rabbits were given a solution of ferrous sulphate by stomach tube before feeding time, the dosage of the drug varying from 0·25 to 3·0 g. per kg. body weight. It was found that with a dosage of 0·75 to 1·0 g. per kg. there was recognizable necrosis of the periportal areas of the liver, and sufficient animals survived to permit study of the lesions to the point of healing. The authors describe their findings in detail. They conclude that in acute ferrous sulphate poisoning in man and animals the outstanding pathological lesion is haemorrhagic periportal necrosis of the liver. The cells in the peripheral portions of the hepatic lobules appear to be more susceptible to damage by large amounts of iron than are those in the central portion, and this, they suggest, may be due to proximity of the peripheral cells to the branches of the portal vein.

Gilbert Forbes

571. **The Value of Barbiturate Estimations in the Diagnosis and Treatment of Barbiturate Intoxication**
J. T. WRIGHT. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **24**, 95–108, Jan., 1955. 2 figs., 36 refs.

Improved techniques for the estimation of the concentration of barbiturates in the blood have shown that a simple quantitative relationship exists between the blood concentration and the effect produced by the drug. The present author contributes further findings which enable observations to be made on certain therapeutic procedures. The clinical material consisted of 27 cases of barbiturate intoxication admitted to the London Hospital, with a further 18 cases of fatal (suicidal) barbiturate poisoning occurring in the London area. Estimations were made by a quantitative spectrophotometric procedure and later exclusively by the method of paper chromatography.

It was shown that a concentration of 10 mg. of barbitone or more per 100 ml. of blood caused deep coma. The corresponding figure for phenobarbitone was 7 to 9 mg., and for the short-acting barbiturates 1 to 3 mg. per 100 ml.; as regards the last-named, blood levels in fatal cases were 2 to 5 mg. per 100 ml. Anoxia and shock greatly increased the depression produced by barbiturates, but tolerance, senility, Parkinsonism, intercurrent disease, and simultaneous administration of other noxious substances such as carbon monoxide, salicylates, and alcohol were also factors to be considered. The short-acting barbiturates were particularly liable to produce shock and pulmonary oedema, and it was these agents which were responsible for most of the deaths outside hospital. Patients reaching hospital tended to be selected in that most of them were suffering from prolonged narcosis produced by long-acting barbiturates. In 9 of the hospital cases treatment with the analeptic picrotoxin was given intravenously at a rate of 3 to 6 mg every half-hour. While this resulted in an increase in the respiration in every case, there was no effect on blood pressure or heart rate, and evidence of earlier arousal attributable to the picrotoxin was obtained in only one case. An instance is given of the generally recognized fact that convulsions produced by picrotoxin usually result in further depression.

Laboratory studies showed that the barbiturates are distributed throughout the body water, so that a fairly accurate estimate of the total dose can be made from determination of the blood level. Shortly after ingestion a high concentration of the drug may be found in the liver, but later it falls to nearly that in the blood. The concentration in the cerebrospinal fluid was found to be significantly lower than that in the blood, even when equilibrium could be assumed to have been reached, and therefore drainage of the spinal fluid (which has been proposed by some authors) cannot be expected to be beneficial. Estimation of barbiturate in the urine by spectrophotometric methods gave unsatisfactory results owing to the presence of interfering chromogens. The findings in a few cases suggest that the renal clearance of barbitone was greater than that of phenobarbitone. Since renal clearance is only slightly increased with higher rates of flow, and since it is difficult to induce diuresis in the early stages of barbiturate poisoning, the author does not recommend forced diuresis, with its attendant hazards. Gastric lavage was found to be of little value if performed more than 4 hours after ingestion of the drug, when most of it has left the stomach.

Norval Taylor

572. **Treatment of Lead Poisoning with Calcium Disodium Versenate**
H. MCC. GILES, C. J. MOORE, and B. M. STILL. *Lancet* [*Lancet*] **1**, 183–185, Jan. 22, 1955. 1 fig., 17 refs.

573. **Arrested Mental Development Induced by Lead-poisoning**
J. W. G. GIBB and J. F. MACMAHON. *British Medical Journal* [*Brit. med. J.*] **1**, 320–323, Feb. 5, 1955. 8 refs.

Anaesthetics

574. **Ether Analgesia during Major Surgery**
J. F. ARTUSIO. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 33–36, Jan. 1, 1955. 2 figs., 11 refs.

Ether analgesia was given to 110 patients subjected to mitral valvotomy and 25 subjected to abdominal surgery at the New York Hospital (Cornell University Medical College). An hour before induction of anaesthesia 0·2 to 0·4 mg. of atropine was administered, this being the only premedication. Repeated injections of 25 mg. of thiopentone were given until the patient indicated that he was becoming sleepy. Administration of nitrous oxide and oxygen, with ether, was then started in a semiclosed system. The pharynx, larynx, and trachea were sprayed with 2% "xylocaine" (lignocaine) and an endotracheal tube, lubricated with 5% lignocaine, was passed into the trachea. The patient was then given 100% oxygen and hyperventilated until consciousness returned. Throughout the operation ether was added when necessary and the pattern of the electroencephalogram (EEG) was used for control purposes.

The author divides the first stage of anaesthesia into three planes, and considers that Plane 3 of Stage 1 is ideal for surgical procedures. Stage-2 anaesthesia (delirium) was often seen when anaesthesia was first induced, but when Stage 3 had once been established and the patient was restored to consciousness and then rendered unconscious again Stage 2 was not seen. Analysis of the EEG tracings showed that a distinct pattern could be associated with analgesia. No untoward reflex disturbances were observed during operation with this light level of anaesthesia.

A. M. Hutton

575. **An Anaesthetist Looks at a Burnt Child**
D. W. SHANNON. *Lancet* [*Lancet*] **1**, 111–115, Jan. 15, 1955. 2 figs., 2 refs.

The author, from the Royal Hospital for Sick Children, Edinburgh, discusses the tasks of the anaesthetist member of a surgical team in the care of the burnt child. He points out that the urgent need for replacing fluid loss in such cases should not obscure the fact that the consequences of anoxia, almost the most common cause of anaesthetic complications, may be serious. The airway is often obstructed from inhalation of hot gases, with desquamation, and tracheotomy or bronchoscopy may be required. In some cases postnasal secretions and crusts impinge on the larynx, or the tongue falls back and obstructs the airway, when passage of a nasopharyngeal tube may be necessary. Anoxia is avoided by giving oxygen at a rate of 2 to 3 litres a minute via a humidifier through a nasal tube, changing nostrils every 12 hours. Diamorphine (heroin) hydrochloride is preferred for restlessness, half the dose, which is proportional to body weight, being given subcutaneously and half intravenously. This drug has proved more effective than morphine or barbiturates.

Between the 10th and 14th days sloughs separate and operative treatment may be required. Because of the high basal metabolic rate in such patients diet is carefully planned and anaesthesia must be so designed that it does not disturb the dietary regimen. Premedication is with atropine, the dose being proportional to age, but no sedatives are given, so that recovery is rapid. In some cases quinalbarbitone is given if necessary. Anaesthesia is induced with cyclopropane and oxygen in the proportion of 3 to 1 and maintained in the proportion of 1 to 3. Cyclopropane is administered with circle absorption to children over 3 years of age and with to-and-fro absorption to children under that age. Endotracheal intubation is carried out as an aid to administration of cyclopropane in cases of burns of the head and neck or dorsal surfaces, or in cases of respiratory embarrassment. The endotracheal tube must be small enough to pass easily without damaging the larynx.

B. L. Finer

576. **Cerebral Blood Flow and Cerebral Oxygen Consumption during Hypothermia**
H. L. ROSOMOFF and D. A. HOLADAY. *American Journal of Physiology* [*Amer. J. Physiol.*] **179**, 85–88, Oct., 1954. 3 figs., 16 refs.

This report from Columbia University College of Physicians and Surgeons and the Presbyterian Hospital, New York, describes investigations into the effects of hypothermia on cerebral blood flow, oxygen consumption, and vascular resistance, systemic blood pressure, and pulse rate which were carried out on dogs under pentobarbitone anaesthesia. A cuffed endotracheal tube was passed, and an automatic positive–negative respirator delivering 200 ml. of pure oxygen 24 times a minute was used. The animals were heparinized. Cerebral blood flow was measured continuously and directly, the arterial supply to the brain being isolated and diverted through a magnetic rotometer. Venous blood samples were obtained from a cannula in the superior sagittal sinus and arterial samples from a carotid artery. The isolated brain was weighed later, and the blood flow expressed in ml. per 100 g. wet weight per minute. Cerebral oxygen consumption was estimated from the blood flow and the arteriovenous oxygen difference. Continuous records of blood pressure and pulse rate were made by means of a bellows manometer joined to a large-bore catheter inserted in the aorta through a femoral artery. Temperature was recorded by means of a mercury thermometer inserted 200 mm. down the oesophagus.

Control readings of cerebral blood flow, blood pressure, and pulse rate were obtained for 30 minutes, and arterial and venous blood samples were drawn for

analysis of the respiratory gases. The dog was then immersed to the shoulders in iced water, and the cerebral blood flow, blood pressure, and pulse rate were noted every 2 minutes. Arterial and venous blood samples were taken again when the body temperature reached 30° and 26° C.

In 10 dogs the cerebral flow varied in proportion with the change in temperature, falling by an average of 6·7% of the flow at 35° C. for every 1° C. fall in temperature. In 8 dogs the mean blood pressure (diastolic+$\frac{1}{3}$ pulse pressure) fell by an average of 4·8 mm. Hg for every 1° C. fall in temperature, though the correlation was not so close in this case. The pulse rate, on the other hand, fell in almost linear proportion with the temperature between 35° and 25° C. Cerebral oxygen consumption was studied in 4 dogs, and varied like the cerebral blood flow with decrease in temperature, but the arteriovenous oxygen differences were almost unchanged. The authors conclude that hypothermia probably causes no hypoxia of brain tissue so long as pulmonary and cardiac function remains adequate. *B. L. Finer*

577. **Analysis of Respiratory Acidosis during Anesthesia**

R. G. ELLISON, L. T. ELLISON, and W. F. HAMILTON. *Annals of Surgery* [*Ann. Surg.*] **141**, 375–382, March, 1955. 1 fig., 31 refs.

The authors report, from the Medical College of Georgia, a study of the changes in respiratory acidosis caused by change of posture, opening of the pleura, or manually assisted respiration. Of the 44 patients studied, 31 were undergoing thoracotomy performed in the lateral position and 13 major general surgical operations performed in the usual supine position. In most of the cases premedication was with pentobarbitone and hyoscine (scopolamine) hydrobromide, induction with hexobarbitone and curare, and maintenance with cyclopropane and oxygen. A cuffed endotracheal tube was connected to a circle absorber and respiration was assisted manually as required. Nitrous oxide and oxygen were employed for a few minutes immediately after induction before introducing cyclopropane and again during the final 10 minutes of anaesthesia, but now using the semi-open method.

Samples of arterial blood were taken for analysis in relation to six arbitrary periods. (1) Before or several days after operation, to serve as a normal control (2) During the first 25 minutes after induction of anaesthesia, when there was a sudden initial increase in carbon dioxide tension (pCO_2), which was considered to be due to the combined action of the barbiturate and relaxant in depressing respiration. A significant finding in this period was a very marked rise in those cases in which anaesthesia was induced with nitrous oxide (mean pCO_2=149·6 mm. Hg in contrast to 69·0 mm. in those in which the gas was not used). (3) During maintenance of anaesthesia with cyclopropane. In this period the mean pCO_2 was 98·3 mm. Hg, and no marked difference was noted between the thoracic and the general surgical cases. (4) During the final 10 minutes on nitrous oxide and before extubation. Here the mean pCO_2 was 175·9 mm. Hg, which was by far the highest level in all groups. A significant rise occurred in 14 cases immediately after changing to nitrous oxide. (5) Within 5 minutes after extubation or removal of the mask. At this moment the pCO_2 fell dramatically to 79·2 mm. Hg. (6) At between 5 and 28 minutes after extubation, when a further fall in pCO_2 to 57·5 mm. Hg occurred, but the value was still well above normal levels. It was further noted that there was little difference in the pCO_2 levels between cases induced with and without nitrous oxide in the 2nd period and again in the 5th and 6th periods.

In regard to posture—although the Trendelenburg, lithotomy, and lateral positions interfere most with ventilation, no significant increase in pCO_2 was found to occur in patients in these positions. The rise in pCO_2 which usually accompanied change to the lateral position invariably occurred before this posture was assumed.

Opening of the pleura caused a mean rise in pCO_2 of 15 mm. Hg in 3 cases, but this could be effectively counteracted by vigorous manual ventilation. Assisted respiration, which was vigorously applied in 4 cases, brought about a fall in pCO_2, but not to normal levels.

Michael Kerr

578. **Potentiation of Pentobarbital Anesthesia by *iso*-Nicotinic Acid Hydrazide and Related Compounds**

A. GOLDIN, D. DENNIS, J. M. VENDITTI, and S. R. HUMPHREYS. *Science* [*Science*] **121**, 364–365, March 11, 1955. 1 fig., 10 refs.

579. **Cyclopropane, Dental Extraction, and Sparks**

J. G. BOURNE and H. J. V. MORTON. *Lancet* [*Lancet*] **1**, 20–22, Jan. 1, 1955. 2 figs., 8 refs.

Having advocated cyclopropane anaesthesia for dental extraction, one of the authors felt compelled to investigate a report that sparks were given off during such operations. In a series of experiments it was found that sparks, visible in daylight, could, in fact, be readily produced by the friction of forceps upon the enamel of teeth and that the number and brilliance of the sparks increased as the oxygen content of the atmosphere was raised. Moreover, these sparks would consistently ignite a mixture of cyclopropane and oxygen if it contained at least 30% oxygen; but below this concentration the mixture could be ignited only by an electric spark or sparks produced by holding a dental forceps against a grindstone. It was therefore concluded that patients were at risk from the explosion hazard if cyclopropane was used in an atmosphere which contained more than 25% oxygen.

Further experiments showed that the exhalations of patients anaesthetized with a mixture of 50% oxygen and 50% cyclopropane (as originally advocated) contained 25% oxygen only after several breaths of air had been taken. The authors then tried a mixture of 50% cyclopropane and equal parts of oxygen and nitrogen. The anaesthesia was indistinguishable from that obtained when pure oxygen was used and the concentration of oxygen in the exhalations did not exceed 23%.

Donald V. Bateman

Radiology

RADIOTHERAPY

580. **Large-volume Radiotherapy**
W. M. LEVITT. *British Journal of Radiology* [*Brit. J. Radiol.*] **28**, 75–86, Feb., 1955. 8 figs.

At St. Bartholomew's Hospital, London, and in private practice the author has treated 500 patients since 1930 by large-volume radiotherapy, which he defines as " any radiotherapeutic procedure in which, by reason of the volume of tissue irradiated, the determining factor in radiation dosage is the constitutional tolerance of the body and not the local tolerance of the tumour bed ". The method used is to raise whole body segments to uniform dosage through 4 bath fields using 250-kV *x* rays with H.V.L. of 2 mm. Cu. Starting with a dose of 50 r to a single field daily, dosage is built up to 100 or 150 r according to the size and tolerance of the patient. A total dose of 1,000 to 1,250 r to all fields is aimed at.

The indications for this treatment are the radiosensitivity and suitable distribution of the disease, while, in addition, reticuloses must be producing sufficient symptoms to justify radiotherapy. Additional masses outside the bath area do not necessarily contraindicate treatment. Radiosensitivity is assessed by giving a dose of 1,200 r over a week to a peripheral mass. If it disappears a higher dose is proved unnecessary, but if not, treatment must be carried to as high a dosage as required. Contraindications are a haemoglobin value of less than 60% and a platelet count of less than 120,000 per c.mm., when it is probably better to deal with the disease piecemeal. Leucopenia, even when accompanied by relative lymphopenia, is not necessarily a contraindication since it may be part of the disease picture and improve with treatment; if all the other indications are present, therefore, treatment should be started and dosage increased cautiously until the leucocyte count starts to rise. Reliance should not be placed upon any one element in assessing safety to proceed with treatment. Large mononuclear cells and lymphocytes should be counted together, since there is often a compensatory increase in the number of the former with a fall in that of the latter. A total leucocyte count of 1,400 per c.mm. or a total mononuclear count of 200 per c.mm. is accepted by the author as a safe minimum.

In the reticuloses, thoracic disease responds better than abdominal disease, and one-fifth of the patients treated have returned to work for periods ranging from 2 months to 2 years or more. In some cases a second course of treatment can be given successfully whereby life may be prolonged for a matter of months. The results might be improved if, with the aid of protective substances, the dosage could be increased by 25%. Of the other diseases treated, the best results have been obtained in cases of abdominal deposits from seminoma, in which 12-, 9-, and 8-year survivals are reported. On the other hand the treatment of metastases in the chest from seminoma has proved disappointing, as has that of advanced ovarian growths. Argentaffin carcinoma of the bowel may prove radiosensitive.

Details of illustrative cases of lymphadenoma, seminoma, ovarian carcinoma, and lymphosarcoma are given, and serial differential blood counts in other cases are tabulated. *G. E. Flatman*

581. **Treatment of the Cornea with a New Lilliput Roentgen Tube.** [In English]
P. J. L. SCHOLTE, C. C. KOK-V. ALPHEN, and B. COMBÉE. *Acta radiologica* [*Acta radiol.* (*Stockh.*)] **42**, 316–328, Oct. 1954. 5 figs., 17 refs.

A description is given of a new miniature *x*-ray tube (45 mm. long and 14 mm. in diameter) which is energized at 25 kV, with a maximum tube current of 200 μA. With this miniature tube the cornea of the rabbit withstood high doses without injury; if, however, the Philips contact tube, which is energized at 50 kV, was used diffuse cataracts developed in all cases within 3 months. Ingrowing vessels in corneal transplants appeared to recede more rapidly in rabbits given irradiation than in the non-irradiated controls. Similar favourable results were obtained in human subjects, both in the treatment of keratitis and in vascularization of corneal transplants. The authors state that the main advantages of this *x*-ray tube are ease of handling, the accuracy with which the beam can be localized, and the resulting increased safety to the deeper parts of the eye. *Jan G. de Winter*

582. **The Treatment of the Carotid-sinus Syndrome by Irradiation**
H. P. GREELEY, M. I. SMEDAL, and W. MOST. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 91–94, Jan. 20, 1955. 2 figs., 17 refs.

A series of 56 cases of carotid-sinus syndrome treated over the past 14 years at the Lahey Clinic, Boston, by irradiation alone is reported. All the cases were considered to be typical, with spontaneous attacks of syncope which were often preceded by auras of various types. Attacks could be induced in all patients by light pressure or massage over the affected sinus. Irradiation was given to each affected sinus as follows: 200 to 220-kV *x* rays, filtration 2 mm. Cu, 1 mm. Al, at a target–skin distance of 50 cm. through a portal of 5 sq. cm. On alternate days 2 or 3 treatments of 200 r were given. If the condition was unilateral the total dose to the carotid sinus was 500 r; if it was bilateral the total dose was 400 r to each sinus. (All doses were measured in air.) In most patients involvement was unilateral.

In 4 cases treatment was too recent for adequate assessment of results; in the remaining 52, none of which

had responded satisfactorily to medical treatment, the follow-up period was at least twice the length of any spontaneous remission. The ages of the patients, 43 men and 9 women, ranged from 18 to 74 years, all except 4 being over 40. Of the 52 patients, 30 had complete remission of symptoms, while in a further 6 there was moderate benefit. A close correlation was noted between objective and subjective signs of improvement. One patient remained free from symptoms for 14 years. Relief was obtained within several days, sometimes within a few hours. Depilation of the treated area was observed in one case, but no other untoward complications were noted.

The relevant literature is discussed, with particular reference to the generally unsatisfactory results of treatment. It is suggested that relief following irradiation is due to a depression of the nerve-endings in the carotid sinus. *A. M. Jelliffe*

583. **The Results of Treatment of Cancer of the Lip, Mouth and Tongue, and of the Breast**
A. NELSON. *Medical Journal of Australia* [*Med. J. Aust.*] 1, 34–39, Jan. 8, 1955. 9 refs.

In this survey the author reviews the results of the treatment of cancer obtained at the Royal Perth Hospital, Perth, Western Australia, since 1930. Four sites are considered—namely, the lip, the oral cavity, the tongue, and the breast.

There were 742 cases of cancer of the lip, of which about 75% could be regarded as cured. A radium or radon implant was the usual treatment. Of 139 cases of carcinoma of the tongue, about 28% were so advanced as to be amenable only to treatment with *x* rays. In this group an over-all 5-year survival rate of 20% was obtained. Cases of cancer at various sites in the oral cavity totalled 86, many of them very advanced; in 48 (56%) of these cases the primary growth was not controlled. There were 700 patients with carcinoma of the breast: the crude 5-year survival rate in this group was about 40% [but no classification in stages is given, the method of selection is not stated, and no details of treatment are given].

The author discusses the treatment of cervical nodes. He is opposed to prophylactic dissection of the neck as a policy. Improved results obtained in recent years are attributed to the use of radon needles, and to adoption of the Manchester dosage system. *E. Stanley Lee*

584. **Experiences with the Use of Radioactive Colloidal Gold in the Treatment of Cancer**
H. B. WHEELER, W. E. JAQUES, and T. W. BOTSFORD. *Annals of Surgery* [*Ann. Surg.*] 141, 208–217, Feb., 1955. 6 figs., 22 refs.

Radioactive colloidal gold (^{198}Au) has been used at the Peter Bent Brigham Hospital (Harvard Medical School), Boston, in the treatment of 42 cases of cancer, its application being intracavitary in 17 cases and interstitial in 25 cases. The maximum penetration of the β particles from ^{198}Au is 3·8 mm. (0·38 mm. mean), and γ rays contribute 5 to 10% of the total radiation. A tumour can be injected interstitially at multiple point sources with ^{198}Au in a fluid medium, and a much larger dose be safely given than by conventional techniques, since the surrounding normal tissues are almost entirely spared. At the same time it is quite possible to leave parts of the tumour unaffected. After intrapleural and intraperitoneal injection, the colloid is dispersed on the serous surfaces; its exact mode of action in reducing the rate of formation of exudate is unknown—it may be due to an effect on tumour nodules scattered over the surface rather than on the serous membrane itself.

Dosage had to be empirical at first, the amounts used being increased with experience. No radiation sickness or overdose effects were seen. The only toxic effect was bone-marrow depression in 4 cases, which was possibly due to the isotope reaching the blood stream on injection into vascular tumours. Small nodules were injected with as much fluid as they would hold; large masses were given up to 100 mc. The intraperitoneal dose used was 100 mc., the intrapleural dose 25 to 50 mc. The fluid was delivered from a lead-shielded syringe with a plunger connected to a calibrated screw.

A group of 14 cases of intra-abdominal cancer were treated at laparotomy by injection of liver nodules or recurrences of gastro-intestinal growth, but adequate injection was hardly possible. More success was gained in treating accessible tumours—of the skin, breast, head, and neck (11 cases). In 2 cases recurrences were controlled for 1 year. Pain due to masses in the neck, breast, or groin was relieved. In 8 cases treated by intrapleural injection the patients were much improved, but none of 9 patients treated by intraperitoneal injection did well, probably because they were all in the terminal stage.

Histologically, a carcinolytic effect, sharply confined to the injected area, was demonstrable. The most marked effect was on epidermoid cancer, the least on secondary adenocarcinoma. The peritoneum was generally thickened by fibrosis, and particles of ^{198}Au were found in histiocytes, serous membranes, regional lymph nodes, liver, spleen, and bone marrow. It is concluded that injection is of no value in treating widely disseminated growths, but can give useful palliation for nodules not easily treatable by surgery or *x* rays. It is the treatment of choice for malignant pleural and peritoneal effusions, but should not normally replace conventional radiotherapy. *J. Walter*

585. **The Use of Radioactive Gold Colloid in Inoperable Carcinoma of the Bladder: Report of 2 Cases**
C. M. NELSON and G. Z. WILLIAMS. *Journal of Urology* [*J. Urol.* (*Baltimore*)] 73, 292–298, Feb., 1955. 3 figs., 2 refs.

Up to 6 months' palliation has been achieved by the authors by the injection of radioactive colloidal gold into inoperable bladder tumours in 2 cases. In the first an ulcerated lesion surrounding the ureteric orifice was approached transvesically through a suprapubic wound and 15 mc. of radioactive colloidal gold in 15 ml. of Ringer's solution with 0·3 ml. of 1 : 1,000 adrenaline was injected into the tumour and surrounding tissues from five syringes, each containing 3 ml. of the solution.

The total tumour dose was 1,140,000 r.e.p. The radiation exposure of the operators and attendants did not exceed 0·1 r. Nursing, in isolation, was restricted to only 15 minutes in each hour for the first 2 days in order to limit the exposure of nurses to less than 0·1 r per day. Precautions were unnecessary by the end of a week. The suprapubic and urethral catheters were removed on the 8th and 13th days respectively. By an identical technique a further 18 mc. was injected into a recurrent tumour 4 months later, the patient dying with extensive growth 3 months after that.

The second patient had previously undergone segmental resection of the bladder for a tumour in the dome, followed by irradiation with intravesical radium and deep *x* rays. A recurrent tumour was injected with 20 mc. of radioactive colloidal gold in 10 ml. of solution. This was carried out through a needle attached to a No. 5 ureteric catheter and passed through a cystoscope. The tumour dose was 1,500,000 r.e.p. This patient obtained permanent relief from bladder pain until his death 6 months later, whereas relief was only temporary in the first case. *G. E. Flatman*

586. **Use of Radioactive Gold in the Treatment of Carcinoma of the Bladder: Report of 8 Cases**
C. M. NELSON. *Southern Medical Journal* [*Sth. med. J. (Bgham, Ala.)*] **48**, 245–250, March, 1955. 4 figs., 10 refs.

587. **Use of Radioactive Cobalt (Co^{60}) in Nylon Sutures in Treatment of Carcinoma of Bladder: Preliminary Report**
V. VERMOOTEN. *Journal of Urology* [*J. Urol. (Baltimore)*] **73**, 280–284, Feb., 1955. 3 figs.

A preliminary report is presented on the use of nylon sutures containing radioactive cobalt (^{60}Co) in the treatment of 7 cases of advanced carcinoma of the bladder. Details of 2 of these cases are given. One patient, who had extensive infiltration of the bladder wall, was well, with no cystoscopic evidence of tumour, 7 months later. The other patient, who had a recurrent tumour following endoscopic resection of the prostate, has remained well for 5 months after treatment with ^{60}Co.

Through a suprapubic transvesical approach the sutures were threaded through the tumour at 1-cm. intervals. The bladder was closed around a suprapubic tube and both ends of each suture brought out through the wound. The sutures were left *in situ* for 7 days. [The dosage is not stated.] *G. E. Flatman*

588. **Further Experience with Intracavitary Radiocobalt for Bladder Tumors**
F. HINMAN, J. W. SCHULTE, and B. V. A. LOW-BEER. *Journal of Urology* [*J. Urol. (Baltimore)*] **73**, 285–291, Feb., 1955. 3 refs.

From the University of California School of Medicine, San Francisco, a report is presented on the treatment of bladder tumours by means of a bead of radioactive cobalt placed in the central channel of a balloon catheter in such a way that when the balloon is inflated the bead lies at its geometric centre. Since June, 1951, when 13 cases treated by this method were reported (Schulte *et al.*, *J. Urol.*, 1952, **67**, 916; *Abstracts of World Medicine*, 1952, **12**, 384) a further 22 have been treated.

Beads of ^{60}Co of 80 to 90 mc. were used in these later cases, and required an exposure time of only 8 to 10 hours compared with 100 hours with 20-mc. beads, but because of the high dose rate, treatment was given in two sessions 7 to 10 days apart. Supplementary deep *x*-ray treatment by means of four 10×10-cm. cross-fire fields, when necessary, was started immediately after completion of the intracavitary irradiation. Surgery is not difficult within 4 months of irradiation. Treatment was based upon a radical-treatment dosage of 7,000 to 8,000 r in 50 to 60 days and a palliative-treatment dosage of 300 to 1,500 r in 1 to 3 weeks. The actual doses given varied from 5,000 to 6,000 r from ^{60}Co, measured at the mucosa, and 3,500 r from *x* rays in 35 to 40 days, estimated at the mid-plane of the abdomen.

Intracavitary cobalt treatment alone was used for 25 patients, and 10 had both cobalt and *x*-ray therapy (2 of the latter failing to complete treatment). The tumours were classified according to Jewell into Groups A, B1, B2, or C depending on whether they were limited to the mucosa, infiltrating either less or more than half the muscle, or had extended beyond the bladder wall. Of 10 patients with lesions of Groups A or B1, 4 have remained free from disease for 4 years. Of 22 patients with lesions of Groups B2 or C, 2 were free of disease 12 and 14 months after treatment, while a third on whom resection was carried out 6 weeks after cobalt treatment was free of disease 18 months later. A detailed analysis of results and morbidity is given.

Intracavitary irradiation of tumours of Groups A and B1 is not regarded as preferable to surgery when there are no more than three lesions 2 to 3 mm. in diameter. The severity of post-irradiation complications depends upon fractionation, and the use of beads of 30 to 40 mc. for periods up to 4 weeks is now under consideration. Superficial lesions can be successfully destroyed whereas infiltrating lesions are only temporarily arrested, though persistent bleeding may be stopped.

G. E. Flatman

RADIODIAGNOSIS

589. **Xeroradiography**
J. F. ROACH and H. E. HILLEBOE. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **73**, 5–9, Jan., 1955. 5 figs.

Xeroradiography is a simple and inexpensive method of recording *x*-ray images which does not require a darkroom or solutions of any kind and for which supplies of sensitized material are not needed, although conventional *x*-ray machines are used.

The name is derived from the Greek word ξηρός, dry, as the process is a photo-electric one requiring no liquids. The plate consists of a sheet of metal such as brass or aluminium on which is deposited a thin layer of selenium. This is encased in a thin wooden frame with a sliding cover. The plate is sensitized by passing closely over its selenium surface a group of wires with a

high positive charge. The charge induced in the selenium is held on its surface owing to its high resistivity in the normal state. The resistivity of selenium, however, is reduced during exposure to *x* rays, so that the charge will then flow into the metal base plate, its dissipation at any given point being proportional to the amount of radiation striking that point. Thus if the charged plate is employed in the same way as a normal *x*-ray plate and then exposed to a cloud of negatively charged powder, this will adhere to each point on the plate in a quantity proportional to the positive charge remaining undischarged at that point and a visible image will be obtained. The record can be made permanent by transferring the powder to an adhesive surface. The plate is rugged and can be cleaned and used many times. Charging requires only a few seconds and powdering 30 to 40 seconds. The effective speed of the xerographic plate lies between those of standard films used with and without intensifying screens. Its resolving power is superior to that of ordinary films, but the contrast given at present is inferior.

The method should prove valuable, especially in large-scale emergency work. *W. D. Nichol*

590. **Use of Planigraphy in Demonstration of Calcification of Heart Valves and its Significance**
L. A. Soloff, J. Zatuchni, and H. Fisher. *Archives of Internal Medicine* [*Arch. intern. Med.*] **95**, 219–223, Feb., 1955. 4 figs., 3 refs.

It is a well-known fact that by means of tomography it is possible to demonstrate calcification of the valves of the heart which is not apparent on fluoroscopy or plain films, but until recently the method has been little used. With the advance of cardiovascular surgery it is obviously important to obtain as much information as possible about the heart before deciding the patient's suitability for operation, and for this purpose the authors believe tomography should be used more frequently. Working at Temple University Medical School, Philadelphia, they have investigated 31 patients, of whom 16 were candidates for mitral valvotomy, while 14 had cardiomegaly and murmurs and one had cardiomegaly with recurrent bouts of atrial tachycardia. Cuts were taken in the left lateral, left posterior oblique, left anterior oblique, and right anterior oblique positions. [The authors do not state any preference for a particular projection, but most of the illustrations to their paper are in the right anterior oblique position.]

The results revealed a surprisingly high yield of findings, in that 26 of the 31 patients were shown to have intracardiac calcification, 9 showing calcification of the mitral valve alone, 3 of the mitral valve and left atrium, 9 of both mitral and aortic valves, and 5 of the aortic valve alone. In 2 cases the demonstration of valvular calcification by tomography was the only evidence of valve disease, and of the 9 patients in whom both the aortic and mitral valves were calcified, only 2 had clinical evidence of combined valvular disease.

The authors suggest that, apart from its use in selection for operation, tomography should be used in all cases of unexplained cardiomegaly in order to elucidate the cause of murmurs of uncertain origin, and also to detect the possible presence of concomitant mitral disease when aortic valvular disease has already been diagnosed.

D. E. Fletcher

591. **Neck Roentgenograms in the Diagnosis of Esophageal Carcinoma**
L. L. Haas and B. Baker. *Radiology* [*Radiology*] **64**, 234–240, Feb., 1955.

Writing from the University of Illinois College of Medicine, Chicago, the authors point out that in the diagnosis of carcinoma of the oesophagus the direct radiological signs are often neglected. They have found that sagittal and lateral radiographs of the neck may be a valuable diagnostic aid, especially (1) in cases in which intramural or extra-oesophageal extension of the tumour exceeds the intraluminal defect as visualized in the barium-filled oesophagus; (2) when there is inadequate barium filling of the oesophagus, either for technical reasons or because of severe dysphagia or vomiting, and when because of stenosis the entire length of the lesion cannot be outlined; (3) when a barium meal is contraindicated because of the danger of haemorrhage or perforation; and (4) when on a plain film made for other reasons there appear signs suggesting the possibility of oesophageal carcinoma.

In interpretation of the radiographs the following signs should be looked for. Deformity of the bases of the piriform sinuses may be seen in the antero-posterior view. Lateral extension of the tumour may be indicated by lateral displacement of the trachea. Posterior extension is evidenced by thickening of the prevertebral soft tissues; this thickening is characteristically wedge-shaped and starts at the cricoid area, the posterior tracheal wall deviating around the mass in the form of an arc. (It is noted that the mass caused by inflammatory lesions in the prevertebral soft tissues is not usually wedge-shaped.) A large lesion may compress the lumen of the trachea. The effect of irradiation can also be followed on lateral films without the use of an opaque medium. *John H. L. Conway-Hughes*

592. **Tumor Outline of Esophageal Carcinoma**
L. L. Haas and B. Baker. *Radiology* [*Radiology*] **64**, 241–248, Feb., 1955. 9 figs., 9 refs.

In this second paper from the University of Illinois College of Medicine, Chicago, the authors point out that the usual method of determining the size of a tumour of the oesophagus by the length of the lesion as indicated by the filling defect in the barium-filled lumen is unsatisfactory, since this procedure fails to outline the tumour in its lateral extent. Visualization of the tumour is aided by the pre-oesophageal location of the trachea, the air content of which is in sharp contrast to the dense tumour tissue, while the latter frequently differs not only from air but also from the surrounding normal tissues.

In the normal oesophagus the wall and peri-oesophageal tissue usually produce a thin, uniform, parallel shadow, the thickness of which depends on the degree of distension of the oesophagus with barium. If a

tumour is present, however, the shadow is neither straight nor uniform. An infiltrating growth may produce a cylindrical or spindle-shaped shadow, while a fungating growth may give a shadow which is irregular, bulging, dense, and sometimes lobulated. A large extra-oesophageal tumour may displace the trachea anteriorly and also compress it. Visualization of a tumour below the carina is usually less favourable, but a secondary bronchus or the air-filled lung may sometimes help to outline the tumour. For differentiation of soft-tissue shadows films made at high voltage are usually the best.

John H. L. Conway-Hughes

593. **Estimation of Liver Function by Cholangiography**
E. SAMUEL, J. GLUCKMAN, and J. BARLOW. *Lancet* [*Lancet*] **1**, 13–15, Jan. 1, 1955. 3 refs.

No single test of liver function is reliable by itself and multiple testing is at present the rule. In a search for a single test of reasonable reliability the authors have investigated, at the Medical Centre, Johannesburg, the value of observing the concentration and rate of excretion in the biliary tract of "biligrafin" (disodium-N-adipic-di-3-amino-2:4:6-triiodo-phenylcarbonate) as the sole means of estimating liver function. To 30 patients 20 ml. of the opaque medium was given intravenously and the density of the resultant shadow in the hepatic and common bile ducts recorded 15 and 40 minutes later on films taken in the prone and prone-oblique positions. Shadows were assessed as good, or as slightly, moderately, or severely impaired, the last category including cases in which there was complete absence of shadows.

These findings were compared with those of 15 well-known tests of liver function, including determination of the serum albumin : globulin ratio and globulin content, the thymol turbidity test, and the Takata–Ara test. (The findings for each patient in each test are presented in tabular form.) In general they showed good correspondence. However, in 7 cases of slight impairment of liver function, as determined by the biochemical tests, cholangiography gave a normal result. In 3 cases of moderate impairment and 3 cases of severe impairment there was exact correlation. The authors conclude that cholangiography with biligrafin is useful in giving a broad estimate of liver function, but is not wholly reliable in detecting minor degrees of damage.

A. M. Rackow

594. **Correlation of Surgical Pathology with Telepaque Cholecystography in Doses of Two Grams**
W. M. WHITEHOUSE. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **100**, 211–215, Feb., 1955.

"Telepaque" (iopanoic acid) has been used in cholecystography for several years and the author feels the time has arrived for its value to be assessed. To do this he has reviewed 124 cases in which cholecystectomy was performed at the University Hospital, Ann Arbor, all of which had been examined by means of a telepaque cholecystogram before operation and in which there had been no marked clinical change pending laparotomy.

In 50 cases (40·3%) the gall-bladder was not visualized. On repetition of the examination a good shadow showing stones was obtained in 2 cases, a faint shadow in 3, while in 11 the gall-bladder was still not outlined; in the other 34 cases the examination was not repeated. At operation 49 of these 50 patients were found to have cholecystitis, gall-stones being present in 45. In only one case was the biliary tract free of intrinsic disease, and this was later shown to be a case of carcinoma of the head of the pancreas.

In 27 cases (21·8%) there was a faint shadow, gall-stones being identified in 21 of them. Re-examination of 4 of these patients disclosed stones in 2 further cases. At operation pathological evidence of chronic cholecystitis was obtained in all 27.

In 44 cases (35·5%) there was good visualization and stones were identified in 42 of them, while operation confirmed the presence of cholecystitis in 43 out of the 44. In 3 further cases there was excellent visualization of the gall-bladder and stones, and these also showed pathological evidence of cholecystitis at operation.

In this series the author calculates that there was 99·2% accuracy in predicting abnormality of the gall-bladder [although this obviously is not the whole story, since clinical features also decide suitability for operation]. The author has found that re-examination in cases of non-visualization and those showing only faint shadows is often worth while, but points out that there is no point in increasing the dose of telepaque beyond 2 g. He emphasizes in conclusion that it is worth remembering that, while poor function does tend to indicate the presence of cholecystitis, an inflamed gall-bladder may on occasion produce an excellent shadow.

D. E. Fletcher

595. **The Roentgen Features of Muscular Dystrophy**
A. LEWITAN and L. NATHANSON. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **73**, 226–234, Feb., 1955. 10 figs., 6 refs.

The radiological features of muscular dystrophy as observed in 35 patients at the Jewish Chronic Disease Hospital, Brooklyn, New York, are described. As a rule the larger muscles of the shoulder and pelvic girdles are affected before the distal limb musculature. Fatty deposits in the musculature produce a characteristic radiological picture similar to that seen in other conditions in which there is muscular atrophy—for example, poliomyelitis. The distinguishing features in muscular dystrophy are the preservation of muscle bulk and an actual increase in size in the pseudohypertrophic form. In neurological disorders with muscle atrophy the amount of subcutaneous fat is increased.

The fatty replacement produces a typical translucent "banding" and feathering of the muscle shadows. As the disease usually develops in early childhood, marked narrowing of the shafts of the long bones is a secondary effect, but growth in length is not disturbed. Severe scoliosis develops in some cases. These skeletal features are, of course, non-specific. At a late stage involvement of the diaphragm is shown by diminished excursions, while basal atelectasis and pneumonia are frequent complications.

Kenneth A. Rowley

CORRECTION:—In Abstract 1111 on page 333 of the April issue, line 26, for "20 ml." read "50 ml."

History of Medicine

596. **The History of Lupus Vulgaris: Its Recognition, Nature, Treatment and Prevention**
B. RUSSELL. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **48**, 127–132, Feb., 1955. 2 figs., 40 refs.

In tracing the history of lupus vulgaris the author states that in the "remote past" lupus, together with various other diseases causing ulceration, was named "herpes esthiomenos" or "formica corrosiva". [He does not mention the possibility that lupus might also have been included in the collective term "leprosy".] The name "lupus" appeared for the first time in the early 14th century. From about the 16th century onwards lupus was regarded as a special form of cancer, sometimes called "noli me tangere", but Willan in 1808 and Cazenave in 1842 demonstrated the separate nature of the two diseases. Tilbury Fox (1864) and Hutchinson (1865) suspected a relationship between lupus and tuberculosis. In 1883 Koch discovered tubercle bacilli in lupus, and in the following year confirmed its tuberculous nature by animal experiments.

The various periods in the treatment of lupus vulgaris are outlined. For many centuries the disease was treated with the cautery and with caustics or with excision and curettage. From the end of the last century onwards treatment with the Finsen lamp became the principal method used. Now the administration of vitamin D_2 (calciferol) has for the first time made the treatment of lupus simple and effective. The value of this vitamin was first reported by Charpy in France in 1943 and by Dowling and Prosser Thomas in Britain in 1945, although already in the middle of the 19th century the French dermatologist Lemery had suggested large doses of cod-liver oil. The recently introduced isoniazid seems to be even more effective than calciferol in the treatment of lupus vulgaris.

The widespread pasteurization of milk (in 1946 52% of cases of lupus vulgaris were attributed to infection with bovine bacilli) and the general improvement in housing and nutrition have contributed largely to the remarkable decline in the incidence of this disease.

A. Fessler

597. **Michael Servetus. His Importance in the History of Medicine**
E. N. KEEN. *South African Medical Journal* [*S. Afr. med. J.*] **29**, 205–208, Feb. 26, 1955. 8 refs.

On October 27, 1553, Michael Servetus was executed for heresy. The theological work which led to his martyrdom, entitled *Christianismi Restitutio*, includes a few pages which have gained for him an honoured place in medical history. But Servetus clearly had no intention of describing the mechanism of the body, save when relevant to the movement of "divine spirit" after it had been inspired as air.

Galenic dogma presupposed the existence of three vital organs, each associated with a system of conduits and charged with its specific spirit or *pneuma*. The liver manufactured blood containing "natural spirit" from digestive products. The right ventricle was part of this system, blood ebbing and flowing from it to the pulmonary artery, whence it was cleansed by respiration. Arteries, connected with the left ventricle, contained blood charged with "vital spirit", manufactured from venous blood changed in some mysterious way during its passage from right to left through invisible interventricular channels. "Animal spirit" was delivered to the body from the brain through the nerves, which were believed to be hollow.

Although Servetus largely acknowledged the Galenic doctrine, he had observed the great size and ramifications of the pulmonary artery, which suggested to him that it did more than simply nourish the lungs. He inferred that blood flowed not through septal pores, but from pulmonary artery to pulmonary vein. He thus deduced the central importance of the lungs.

Viewed within the context of 16th-century thought, Servetus's functional conclusions were orthodox and their agreement with modern knowledge largely accidental. That the lungs were the site of blood transfer from right to left, instead of interventricular pores, did not much interfere with the Galenic concept of circulatory dynamics. But his accurate anatomical observations, coupled with the courageous proclamation of his views in an intolerant age, have earned him his place in medical history.

M. Sandler

598. **Rudolf Virchow and Recklinghausen's Disease.** (Rudolf Virchow und die Recklinghausensche Krankheit)
E. HOFFMANN. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **80**, 293–295, Feb. 25, 1955. 3 figs., 7 refs.

The author reproduces 3 pictures of classic cases of Recklinghausen's disease, the first being that of a 47-year-old woman which was published in Virchow's *Die krankhaften Geschwuelste* in 1863. Histological examination showed bands of fibres arranged as a fine network in poorly vascularized connective tissue. Virchow, however, failed to demonstrate nerve elements in the tumours, nor did he note the mental deficiency and pigmented naevi which are so often found in this condition.

The other two pictures are reproduced from Recklinghausen's monograph, published in 1882. In both patients, a 55-year-old woman and a 47-year-old man, Recklinghausen demonstrated the presence of nerve fibrils in the tumours by staining with osmium. The condition had been noted previously and was variously described as fibroma molluscum and as elephantiasis mollis. The first description is attributed to Tilesius (1793).

H. F. Reichenfeld